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(54) Title: HUMAN PROTEINS HAVING HYDROPHOBIC DOMAINS AND DNAs ENCODING THESE PROTEINS

(57) Abstract: The present invention provides human proteins having hydrophobic domains, DNAs encoding these proteins, expression vectors for these DNAs, transformed eukaryotic cells expressing these DNAs and antibodies directed to these proteins.

#### DESCRIPTION

# Human Proteins Having Hydrophobic Domains and DNAs Encoding These Proteins

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#### TECHNICAL FIELD

The present invention relates to human proteins having hydrophobic domains, DNAs encoding these proteins, expression vectors for these DNAs, eukaryotic cells expressing these DNAs and antibodies directed to these proteins. The proteins of the present invention can be employed as pharmaceuticals or as antigens for preparing antibodies directed to these proteins. The human cDNAs of the present invention can be utilized as probes for genetic diagnosis and gene sources for gene therapy. Furthermore, the cDNAs can be utilized as gene sources for producing the proteins encoded by these cDNAs in large quantities. Cells into which these genes are introduced to express secretory proteins or membrane proteins in large quantities can be utilized for detection of the corresponding receptors or ligands, screening of novel small molecule pharmaceuticals and the like. The antibodies of the present invention can be utilized for the detection, quantification, purification and the like of the proteins of the present invention.

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#### BACKGROUND ART

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Cells secrete many proteins extracellularly. These secretory proteins play important roles in the proliferation control, the differentiation induction, the material transport, the biophylaxis, and the like of the cells. Unlike intracellular proteins, the secretory proteins exert their actions outside the cells. Therefore, they can be administered in the intracorporeal manner such as the they possess hidden drip, and injection or the potentialities as pharmaceuticals. In fact, a number of human secretory proteins such as interferons, interleukins, erythropoietin, thrombolytic agents and the like are pharmaceuticals. addition, currently employed as In secretory proteins other than those described above are undergoing clinical trials for developing their use as pharmaceuticals. It is believed that the human cells produce many unknown secretory proteins. Availability of these secretory proteins as well as genes encoding them is expected to lead to development of novel pharmaceuticals utilizing them.

On the other hand, membrane proteins play important roles, as signal receptors, ion channels, transporters and the like, in the material transport and the signal transduction through the cell membrane. Examples thereof include receptors for various cytokines, ion

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channels for the sodium ion, the potassium ion, the chloride ion and the like, transporters for saccharides, amino acids and the like. The genes for many of them have already been cloned. It has been clarified that abnormalities in these membrane proteins are involved in a number of previously cryptogenic diseases. Therefore, discovery of a new membrane protein is expected to lead to elucidation of the causes of many diseases, and isolation of new genes encoding the membrane proteins has been desired.

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Heretofore, due to difficulty in the purification from human cells, many of these secretory proteins and membrane proteins have been isolated by genetic approaches. A general method is the so-called expression cloning method, in which a cDNA library is introduced into eukaryotic cells to express cDNAs, and the cells secreting, or expressing on the surface of membrane, the protein having the activity of interest are then screened. However, only genes for proteins with known functions can be cloned by using this method.

In general, a secretory protein or a membrane protein possesses at least one hydrophobic domain within the protein. After synthesis on ribosomes, such domain works as a secretory signal or remains in the phospholipid membrane to be entrapped in the membrane. Accordingly, if the existence of a highly hydrophobic domain is observed in the amino acid sequence of a protein encoded by a cDNA when the

whole base sequence of the full-length cDNA is determined, it is considered that the cDNA encodes a secretory protein or a membrane protein.

#### 5 OBJECTS OF INVENTION

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The main object of the present invention is to provide novel human proteins having hydrophobic domains, DNAs coding for these proteins, expression vectors for these DNAs, transformed eucaryotic cells that are capable of expressing these DNAs and antibodies directed to these proteins.

#### SUMMARY OF INVENTION

As the result of intensive studies, the present inventors have successfully cloned cDNAs encoding proteins having hydrophobic domains from the human full-length cDNA bank, thereby completing the present invention. Thus, the present invention provides a human protein having hydrophobic domain(s), namely a protein comprising any one of amino acid sequences selected from the group consisting of SEQ ID NOS: 1 to 10, 31 to 40, 61 to 70, 91 to 100 and 121 to 130. Moreover, the present invention provides a DNA encoding said protein, exemplified by a cDNA comprising any one of base sequences selected from the group consisting of SEQ ID NOS: 11 to 30, 41 to 60, 71 to 90, 101 to 120 and 131

to 150, an expression vector that is capable of expressing said DNA by in vitro translation or in eukaryotic cells, a transformed eukaryotic cell that is capable of expressing said DNA and of producing said protein, and an antibody directed to said protein.

This object as well as other objects and advantages of the present invention will become apparent to those skilled in the art from the following description with reference to the accompanying drawings.

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#### BRIEF DESCRIPTION OF DRAWINGS

Figure 1: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03613.

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Figure 3: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03935.

Figure 4: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10755.

Figure 5: A figure depicting the 25 hydrophobicity/hydrophilicity profile of the protein

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encoded by clone HP10760.

Figure 6: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10764.

Figure 7: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10768.

Figure 8: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10769.

Figure 9: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10784.

Figure 10:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10786.

Figure 11:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03727.

Figure 12:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03801.

Figure 13:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03883.

figure depicting the Figure 14: A hydrophobicity/hydrophilicity profile of protein the encoded by clone HP03913. the figure depicting Figure 15: A hydrophobicity/hydrophilicity profile of the protein 5 encoded by clone HP10753. the depicting Figure 16: A figure hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10758. figure depicting the o Figure 17: A 10 hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10771. figure depicting the Figure 18: A hydrophobicity/hydrophilicity profile of protein the encoded by clone HP10778. 15 depicting the Figure 19: A figure hydrophobicity/hydrophilicity profile of the encoded by clone HP10781. figure depicting the Figure 20:A hydrophobicity/hydrophilicity profile of the protein 20 encoded by clone HP10785. the figure . depicting Figure 21:A hydrophobicity/hydrophilicity profile of protein the encoded by clone HP03878. the figure depicting Figure 22:A 25

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hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03884.

Figure 23:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03934.

Figure 24: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03949.

Figure 25: A figure depicting the

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encoded by clone HP03959.

Figure 26: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03983.

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Figure 28: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10775.

Figure 29: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10782.

Figure 30:A figure depicting the hydrophobicity/hydrophilicity profile of the protein.

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figure depicting Figure 31:A the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03977. figure depicting the Figure 32:A hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10649. Figure 33:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10779. Figure 34: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10790. figure Figure 35: A depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10793. figure depicting Figure 36: A the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10794. Figure 37: A figure depicting hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10797. Figure 38: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10798.

Figure 39: A figure

depicting

the

hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10800.

Figure 40:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10801.

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Figure 41:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03596.

Figure 42:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03882.

Figure 43:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03903.

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Figure 45: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP03978.

Figure 46: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10735.

Figure 47: A figure depicting the 25 hydrophobicity/hydrophilicity profile of the protein

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encoded by clone HP10750.

Figure 48: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10777.

Figure 49: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10780.

Figure 50:A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10795.

#### DETAILED DESCRIPTION OF THE INVENTION

obtained, for example, by a method for isolating proteins from human organs, cell lines or the like, a method for preparing peptides by the chemical synthesis based on the amino acid sequence of the present invention, or a method for producing proteins by the recombinant DNA technology using the DNAs encoding the hydrophobic domains of the present invention. Among these, the method for producing proteins by the recombinant DNA technology is preferably employed. For example, the proteins can be expressed in vitro by preparing an RNA by in vitro transcription from a vector having the cDNA of the present invention, and then carrying out in vitro translation using this RNA as a

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template. Alternatively, incorporation of the translated region into a suitable expression vector by the method known in the art may lead to expression of the encoded protein in large quantities in prokaryotic cells such as *Escherichia coli* and *Bacillus subtilis*, or eukaryotic cells such as yeasts, insect cells and mammalian cells.

In the case where the protein of the present invention is produced by expressing the DNA by in vitro translation, the protein of the present invention can be produced in vitro by incorporating the translated region of this cDNA into a vector having an RNA polymerase promoter, and then adding the vector to an in vitro translation system such as a rabbit reticulocyte lysate or a wheat germ extract, which contains an RNA polymerase corresponding to the promoter. The RNA polymerase promoters are exemplified by T7, T3, SP6 and the like. The vectors containing promoters for these RNA polymerases are exemplified by pKA1, pCDM8, pT3/T7 18, pT7/3 19, pBluescript II and the like. Furthermore, the protein of the present invention can be expressed in the secreted form or the form incorporated in the microsome membrane when a canine pancreas microsome or the like is added to the reaction system.

In the case where the protein of the present invention is produced by expressing the DNA in a microorganism such as *Escherichia coli*, a recombinant

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expression vector in which the translated region of the cDNA of the present invention is incorporated into an expression vector having an origin which is capable of replicating in the microorganism, a promoter, a ribosome-binding site, a cDNA-cloning site, a terminator and the like is constructed. After transformation of the host cells with this expression vector, the resulting transformant is cultured. Thus, the protein encoded by the cDNA can be produced in large quantities in the microorganism. In this case, a protein adding an initiation codon and a termination codon in front of and behind the selected translated region and expressing the protein. Alternatively, the protein can be expressed as a fusion protein with another protein. Only the portion of the protein encoded by the cDNA can be obtained by cleaving this fusion protein with a suitable protease. The expression vectors for Escherichia coli are exemplified by the pUC series, pBluescript II, the pET expression system, the pGEX expression system and the like.

In the case where the protein of the present invention is produced by expressing the DNA in eukaryotic cells, the protein of the present invention can be produced as a secretory protein, or as a membrane protein on the surface of cell membrane, by incorporating the translated region of the cDNA into an expression vector for eukaryotic

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cells that has a promoter, a splicing region, a poly(A) addition site and the like, and then introducing the vector into the eukaryotic cells. The expression vectors are exemplified by pKA1, pED6dpc2, pCDM8, pSVK3, pMSG, pSVL, pBK-CMV, pBK-RSV, EBV vectors, pRS, pYES2 and the like. Examples of eukaryotic cells to be used in general include mammalian cultured cells such as monkey kidney COS7 cells and Chinese hamster ovary CHO cells, budding yeasts, fission yeasts, silkworm cells, and Xenopus oocytes. Any eukaryotic cells may be used as long as they are capable of expressing the proteins of the present invention. The expression vector can be introduced into the eukaryotic cells by using a method known in the art such as the electroporation method, the calcium phosphate method, the liposome method and the DEAE-dextran method.

After the protein of the present invention is expressed in prokaryotic cells or eukaryotic cells, the protein of interest can be isolated and purified from the culture by a combination of separation procedures known in the art. Examples of the separation procedures include treatment with a denaturing agent such as urea or a detergent, sonication, enzymatic digestion, salting-out or dialysis, centrifugation, solvent precipitation, ultrafiltration, gel filtration, SDS-PAGE, isoelectric chromatography, hydrophobic focusing, ion-exchange

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chromatography, affinity chromatography and reverse phase chromatography.

The proteins of the present invention also include peptide fragments (of 5 amino acid residues or more) containing any partial amino acid sequences in the amino acid sequences represented by SEQ ID NOS: 1 to 10, 31 to 40, 61 to 70, 91 to 100 and 121 to 130. These peptide fragments can be utilized as antigens for preparation of antibodies. Among the proteins of the present invention, those having the signal sequences are secreted in the form of mature proteins after the signal sequences are removed. Therefore, these mature proteins shall come within the scope of the protein of the present invention. The N-terminal amino acid sequences of the mature proteins can be easily determined by using the method for the determination of cleavage site of a signal sequence [JP-A 8-187100]. Furthermore, some membrane proteins undergo the processing on the cell surface to be converted to the secreted forms. Such proteins or peptides in the secreted forms shall also come within the scope of the protein of the present invention. In the case where sugar chain-binding sites are present in the amino acid sequences of the proteins, expression of the proteins in appropriate eukaryotic cells affords the proteins to which sugar chains are added. Accordingly, such proteins or peptides to which sugar chains are added shall also come . 5

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within the scope of the protein of the present invention.

The DNAs of the present invention include all the DNAs encoding the above-mentioned proteins. These DNAs can be obtained by using a method for chemical synthesis, a method for cDNA cloning and the like.

The cDNAs of the present invention can be cloned, for example, from cDNA libraries derived from the human cells. The cDNAs are synthesized by using poly(A) + RNAs extracted from human cells as templates. The human cells may be cells delivered from the human body, for example, by the operation or may be the cultured cells. The cDNAs can be synthesized by using any method such as the Okayama-Berg method [Okayama, H. and Berg, P., Mol. Cell. Biol. 2: 161-170 (1982)], the Gubler-Hoffman method [Gubler, U. and Hoffman, J., Gene 25: 263-269 (1983)] and the like. However, it is desirable to use the capping method [Kato, S. et al., Gene 150: 243-250 (1994)], as exemplified in Examples, in order to obtain a full-length clone in an effective manner. In addition, commercially available human cDNA libraries can be utilized. The cDNAs of the present invention can be the CDNA libraries by synthesizing cloned from oligonucleotide on the basis of base sequences of any portion in the cDNA of the present invention and screening the cDNA libraries using this oligonucleotide as a probe for colony or plaque hybridization according to a method known

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in the art. In addition, the cDNA fragments of the present invention can be prepared from an mRNA isolated from human cells by the RT-PCR method in which oligonucleotides which hybridize with both termini of the cDNA fragment of interest are synthesized, which are then used as the primers.

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The cDNAs of the present invention are characterized in that they comprise any one of the base sequences represented by SEQ ID NOS: 11 to 20, 41 to 50, 71 to 80, 101 to 110 and 131 to 140 or the base sequences represented by SEQ ID NOS: 21 to 30, 51 to 60, 81 to 90, 111 to 120 and 141 to 150. Table 1 summarizes the clone number (HP number), the cells from which the cDNA clone was obtained, the total number of bases of the cDNA, and the number of the amino acid residues of the encoded protein, for each of the cDNAs.

Table 1

Seq	 Sequence		HP No.	Cell	Number	Number of	
					of	amino	
				<del></del>	bases	acids	
1,	11,	21	HP03613	Kidney	2865	578	
2,	12,	22	HP03700	Kidney	3323	243	
3,	13,	23	нР03935	Kidney	1585	461	
4,	14,	24	HP10755	Kidney	2122	647	
5,	15,	25	HP10760	Kidney	1775	446	
6,	16,	26	HP10764	Kidney	1372	197	
7,	17,	27	HP10768	Kidney	2074	540	
8,	18,	28	HP10769	Kidney	2252	442	
9,	19,	29	HP10784	Kidney	1461	262	
10,	20,	30	HP10786	Kidney	1122	152	
31,	41,	51	HP03727	Kidney	1617	335	
32,	42,	52	HP03801	Umbilical cord blood	1749	208	
33,	43,	53	HP03883	Kidney	1402	406	
34,	44,	54	HP03913	Kidney	2474	618	
35,	45,	55	HP10753	Umbilical cord blood	3296	208	
36,	46,	56	HP10758	Kidney	1818	502	
37,	47,	57	HP10771	Kidney	1646	336	
38,	48,	58	HP10778	Kidney	1416	340	
39,	49,	59	HP10781	Kidney	1927	223	
40,	50,	60	HP10785	Kidney	1419	309	
61,	71,	81	HP03878	Kidney	2016	599	
62,	72,	82	HP03884	Kidney	1446	81	
63,	73,	83	HP03934	Kidney	2467	654	
64,	74,	84	HP03949	Kidney	1450	390	
65,	75,	85	HP03959	Kidney	1897	452	

Table 1 (continued)

Sequence	No.	HP No.	Cell	Number of	Number of
			·	bases	acids
66, 76,	86	HP03983	Kidney	1856	490
67, 77.,	87	HP10745	Umbilical cord blood	2173	392
68, 78,	88	HP10775	Kidney	1934	538
69, 79,	89	HP10782	Kidney	1880	102
70, 80,	90	HP10787	Kidney	2295	442
91, 101,	111	HP03977	Kidney	1894	227
92, 102,	112	HP10649	KB	2413	352
93, 103,	113	HP10779	Kidney .	2376	130
94, 104,	114	HP10790	Kidney	1155	330
95, 105,	115	HP10793	Kidney	1329	350
96, 106,	116	HP10794	Kidney	1387	113
97, 107,	117	HP10797	Kidney	1158	189
98, 108,	118	HP10798	Kidney	1106	277
99, 109,	119	HP10800	Kidney	1907	274
100, 110,	120	HP10801	Kidney	1816	390
121, 131,	141	HP03696	Umbilical cord blood	1961	395
122, 132,	142	HP03882	Kidney	2194	550
123, 133,	143	нр03903	Kidney	2753	218
124, 134,	144	HP03974	Kidney	2085	596
125, 135,	145	HP03978	Kidney	2208	467
126, 136,	146	HP10735	Umbilical cord blood	2044	476
127, 137,	147	HP10750	Umbilical cord blood	2176	449
128, 138,	148	HP10777	Kidney	1363	105
129, 139,	149	HP10780	Kidney	1043	81
130, 140,	150	HP10795	Kidney	2435	552

The same clones as the cDNAs of the present

invention can be easily obtained by screening the cDNA libraries constructed from the human cell lines or human tissues utilized in the present invention using an oligonucleotide probe synthesized on the basis of the base sequence of the cDNA provided in any one of SEQ ID NOS: 11 to 30, 41 to 60, 71 to 90, 101 to 120 and 131 to 150.

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In general, the polymorphism due to the individual differences is frequently observed in human genes. Accordingly, any cDNA in which one or plural nucleotides are added, deleted and/or substituted with other nucleotides in SEQ ID NOS: 11 to 30, 41 to 60, 71 to 90, 101 to 120 and 131 to 150 shall come within the scope of the present invention.

Similarly, any protein in which one or plural amino acids are added, deleted and/or substituted with other amino acids resulting from the above-mentioned changes shall come within the scope of the present invention, as long as the protein possesses the activity of the protein having any one of the amino acid sequences represented by SEQ ID NOS: 1 to 10, 31 to 40, 61 to 70, 91 to 100 and 121 to 130.

The cDNAs of the present invention also include cDNA fragments (of 10 bp or more) containing any partial base sequence in the base sequences represented by SEQ ID NOS: 11 to 20, 41 to 50, 71 to 80, 101 to 110 and 131 to 140 or in the base sequences represented by SEQ ID NOS: 21 to 30, 51 to 60, 81 to 90, 111 to 120 and 141 to 150. Also, DNA

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fragments each consisting of a sense strand and an antisense strand shall come within this scope. These DNA fragments can be utilized as the probes for the genetic diagnosis.

The antibody of the present invention can be obtained from a serum after immunizing an animal using the protein of the present invention as an antigen. A peptide that is chemically synthesized based on the amino acid sequence of the present invention and a protein expressed in eukaryotic or prokaryotic cells can be used as an antigen. Alternatively, an antibody can be prepared by introducing the above-mentioned expression vector for eukaryotic cells into the muscle or the skin of an animal by injection or by using a gene gun and then collecting a serum therefrom [JP-A 7-313187]. Animals that can be used include a mouse, a rat, a rabbit, a goat, a chicken and the like. A monoclonal antibody directed to the protein of the present invention can be produced by fusing B cells collected from the spleen of the immunized animal with myelomas to generate hybridomas.

In addition to the activities and uses described above, the polynucleotides and proteins of the present invention may exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by

and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

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The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for highthroughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction.

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Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

#### 15 <u>Nutritional Uses</u>

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or

polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

# Cytokine and Cell Proliferation/Differentiation Activity

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A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e and CMK.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In

Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Bertagnolli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152: 1756-1761, 1994.

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Assays for cytokine production and/or spleen cells, lymph node cells proliferation of thymocytes include, without limitation, those described in: a Polyclonal T cell stimulation, Kruisbeek, A.M. and Shevach, E.M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human Interferon y, Schreiber, R.D. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 336:690-692, 1988;

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Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6-Nordan, R. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11 - Bennett, F., Giannotti, J., Clark, S.C. and Turner, K. J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9 - Ciarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun.

11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

#### Immune Stimulating or Suppressing Activity

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A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases causes by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania and various fungal infections such malaria spp. candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

Autoimmune disorders which may be treated using a

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protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic rheumatoid arthritis, autoimmune lupus erythematosus, pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitis, myasthenia graft-versus-host disease and autoimmune gravis, inflammatory eye disease. Such a protein of the present invention may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. Other immune is suppression desired in which conditions, (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

Using the proteins of the invention it may also be possible to immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an response already in progress involve or mav preventing the induction of immune response. an functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable WO 01/49728

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from immunosuppression in that it is generally antigenspecific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as , for example, B7)), e.g.; preventing high level lymphokine synthesis by activated T cells, will situations of tissue, skin and organ useful in be transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. rejection of the tissue transplants, in Typically, transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (e.g., B7-1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding

costimulatory signal. Blocking B lymphocyte antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

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Blocking antigen function mav also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor: ligand interactions of B lymphocyte antigens can be 0 used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating useful therapy. be in responses, may also immune Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

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Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and

thereby activate, T cells in vivo.

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application, up regulation or another enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II

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molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I lphachain protein and  $\beta_2$  microglobulin protein or an MHC class II  $\alpha$  chain protein and an MHC class II  $\beta$  chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated invariant chain, can also such as the protein, cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan,

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A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et 5 al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 10 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowmanet al., J. Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994. 15

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In vitro antibody production, Mond, J.J. and Brunswick, M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will

identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

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Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al., Journal of 20 Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

Assays for lymphocyte survival/apoptosis (which

will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

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Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

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## Hematopoiesis Regulating Activity

A protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby

indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation and granulocytes such as myeloid cells 5 of traditional activity) monocytes/macrophages (i.e., CSF useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting proliferation megakaryocytes of and growth the consequently of platelets thereby allowing prevention or 10 disorders such various platelet treatment of thrombocytopenia, and generally for use in place of or complementary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-15 mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without anemia and paroxysmal nocturnal aplastic limitation, hemoglobinuria), as well as in repopulating the stem cell 20 compartment post irradiation/chemotherapy, either in-vivo or conjunction bone with ex-vivo (i.e., in cell peripheral progenitor with transplantation or transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy. 25

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The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M.G. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I.K. and Briddell, R.A. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay,

Ploemacher, R.E. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

#### Tissue Growth Activity

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A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial

defects, and also is useful in cosmetic plastic surgery.

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A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo

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tissue formation induced by tendon/ligament-like composition of the present invention contributes to the repair of congenital, trauma induced; or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, differentiation of progenitors of tendoninduce ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel ligament defects. The syndrome tendon or and other compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

The protein of the present invention may also be neural cells of useful for proliferation regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral injuries, peripheral nerve system, such as nervous

peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager Further syndrome. conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, spinal cord disorders, head trauma such as cerebrovascular diseases as stroke. Peripheral such neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

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Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds and the like.

It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A

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protein of the invention may also exhibit angiogenic activity.

A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. W095/16035 (bone, cartilage, tendon); International Patent Publication No. W095/05846 (nerve, neuronal); International Patent Publication No. W091/07491 (skin, endothelium).

Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

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A protein of the present invention may also exhibit activin- or inhibin-related activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins and are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin  $\alpha$  family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin- $\beta$  group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for activin/inhibin activity include,

without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Forage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

# Chemotactic/Chemokinetic Activity

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A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, and/or endothelial epithelial eosinophils, Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction lymphocytes, of monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells.

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Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

5 The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25: 1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153: 1762-1768, 1994.

# Hemostatic and Thrombolytic Activity

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protein is expected to be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke)).

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

# Receptor/Ligand Activity

A protein of the present invention may also
demonstrate activity as receptors, receptor ligands or
inhibitors or agonists of receptor/ligand interactions.

Examples of such receptors and ligands include, without
limitation, cytokine receptors and their ligands, receptor
kinases and their ligands, receptor phosphatases and their
ligands, receptors involved in cell-cell interactions and

their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22), Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenborg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

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Proteins of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cellcell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities 10 can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, hyperacute rejection, nephritis, complement-mediated cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

## Tumor Inhibition Activity

In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities. A protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth.

## Other Activities

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A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body shape (such as, for example, breast part size or augmentation or diminution, change in bone form or shape); effecting biorhythms or cardiac cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization,

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storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent  $^{\circ}$ behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulinlike activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

#### Examples

20 The present invention is specifically illustrated in more detail by the following Examples, but Examples are not intended to restrict the present invention. The basic procedures with regard to the recombinant DNA and the enzymatic reactions were carried out according to the

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literature ["Molecular Cloning. A Laboratory Manual", Cold Spring Harbor Laboratory, 1989]. Unless otherwise stated, restriction enzymes and various modifying enzymes to be used were those available from Takara Shuzo. The buffer compositions and the reaction conditions for each of the enzyme reactions were as described in the attached instructions. The cDNA synthesis was carried out according to the literature [Kato, S. et al., Gene 150: 243-250 (1994)].

(1) Selection of cDNAs Encoding Proteins Having
Hydrophobic Domains

The cDNA library of epidermoid carcinoma cell line KB (W098/11217), and the cDNA libraries constructed from human kidney mRNA (Clontech) and human umbilical cord blood mRNA were used as cDNA libraries.

Full-length cDNA clones were selected from the respective libraries and the whole base sequences thereof were determined to construct a homo-protein cDNA bank consisting of the full-length cDNA clones. The hydrophobicity/hydrophilicity profiles were determined for the proteins encoded by the full-length cDNA clones registered in the homo-protein cDNA bank by the Kyte-Doolittle method [Kyte, J. & Doolittle, R. F., J. Mol. Biol. 157: 105-132 (1982)] to examine the presence or absence of a hydrophobic domain. A clone that has a hydrophobic region

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being assumed as a secretory signal or a transmembrane domain in the amino acid sequence of the encoded protein was selected as a clone candidate.

(2) Protein Synthesis by In Vitro Translation

The plasmid vector bearing the cDNA of the present invention was used for in vitro transcription/translation with a  $T_N T$  rabbit reticulocyte lysate kit (Promega). In this case, [35]methionine was added to label the expression product with a radioisotope. Each of the reactions was carried out according to the protocols attached to the kit. Two micrograms of the plasmid was subjected to the reaction at 30°C for 90 minutes in the reaction solution of a total volume of 25  $\mu$ l containing 12.5  $\mu$ l  $\mu$  of  $T_NT$  rabbit reticulocyte lysate, 0.5 µl of a buffer solution (attached to the kit), 2 µl of an amino acid mixture (without methionine), 2  $\mu$ l of [35S]methionine (Amersham) (0.37 MBq/ $\mu$ l), 0.5 µl of T7 RNA polymerase, and 20 U of RNasin. The experiment in the presence of a membrane system was carried out by adding 2.5  $\mu l$  of a canine pancreas microsome fraction (Promega) to the reaction system. 2  $\mu l$  of the SDS sampling buffer (125 mM Tris-hydrochloride buffer, pH 6.8, 120 mM 2mercaptoethanol, 2% SDS solution, 0.025% Bromophenol Blue and 20% glycerol) was added to 3 µl of the reaction solution. The resulting mixture was heated at 95°C for 3 minutes and then subjected to SDS-polyacrylamide gel electrophoresis.

The molecular weight of the translation product was determined by carrying out the autoradiography.

## (3) Expression in COS7

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Escherichia coli cells harboring the expression vector for the protein of the present invention were cultured at 37°C for 2 hours in 2 ml of the 2 x YT culture medium containing 100  $\mu$ g/ml of ampicillin, the helper phage M13K07 (50  $\mu$  1) was added thereto, and the cells were then cultured at 37°C overnight. Single-stranded phage particles were obtained by polyethylene glycol precipitation from a supernatant separated by centrifugation. The particles were suspended in 100  $\mu$ l of 1 mM Tris-0.1 mM EDTA, pH 8 (TE).

The cultured cells derived from monkey kidney, COS7, were cultured at 37°C in the presence of 5% CO<sub>2</sub> in the Dulbecco's modified Eagle's medium (DMEM) containing 10% fetal calf serum. 1 x 10<sup>5</sup> COS7 cells were inoculated into a 6-well plate (Nunc, well diameter: 3 cm) and cultured at 37°C for 22 hours in the presence of 5% CO<sub>2</sub>. After the medium was removed, the cell surface was washed with a phosphate buffer solution followed by DMEM containing 50 mM Trishydrochloride (pH 7.5) (TDMEM). A suspension containing 1 µl of the single-stranded phage suspension, 0.6 ml of the DMEM medium and 3 µl of TRANSFECTAM<sup>TM</sup> (IBF) was added to the cells and the cells were cultured at 37°C for 3 hours in the presence of 5% CO<sub>2</sub>. After the sample solution was removed,

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the cell surface was washed with TDMEM, 2 ml per well of DMEM containing 10% fetal calf serum was added, and the cells were cultured at 37°C for 2 days in the presence of 5% CO<sub>2</sub>. After the medium was exchanged for a medium containing [35S]cysteine or [35S]methionine, the cells were cultured for one hour. After the medium and the cells were separated each other by centrifugation, proteins in the medium fraction and the cell membrane fraction were subjected to SDS-PAGE.

## (4) Preparation of Antibodies

A plasmid vector containing the cDNA of the present invention was dissolved in a phosphate buffer solution (PBS: 145 mM NaCl, 2.68 mM KCl, 8.09 mM Na2HPO4, 2 mM  $KH_2PO_4$ , pH 7.2) at a concentration of 2  $\mu g/\mu l$ . 25  $\mu l$  each (a total of 50 µl) of the thus prepared plasmid solution in PBS was injected into the right and left musculi quadriceps femoris of three mice (ICR line) using a 26 guage needle. After similar injections were repeated for one month at intervals of one week, blood was collected. The collected blood was stored at 4°C overnight to coagulate the blood, and then centrifuged at 8,000 x g for five minutes to obtain a supernatant. NaN, was added to the supernatant to a concentration of 0.01% and the mixture was then stored at 4°C. The generation of an antibody was confirmed by immunostaining of COS7 cells into which the corresponding vector had been introduced, or by Western blotting using a

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cell lysate or a secreted product.

#### (5) Clone Examples

<HP03613> (SEQ ID NOS: 1, 11, and 21)

Determination of the whole base sequence of the cDNA insert of clone HP03613 obtained from cDNA library of human kidney revealed the structure consisting of a 337-bp 5'-untranslated region, a 1737-bp ORF, and a 791-bp 3'untranslated region. The ORF encodes a protein consisting of 578 amino acid residues and there existed eleven putative 1 depicts the Figure domains. transmembrane hydrophobicity/hydrophilicity profile, obtained by the Kytemethod, of the present protein. Doolittle translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to mouse organic cation transporter-like protein (Accession No. BAA23875). Table 2 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and mouse organic cation transporter-like protein (MT). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology

of 70.4% in the entire region.

Table 2

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- - HP LQMAVMGTAAAFAPAFPVYCLFRFLLAFAVAGVMMNTGTLRRSLTWRHAGGLHAGSRAEP

    \* .. \* \*\*\*\*\* \*. \*\*. \*\*\*\*\*\*\* \*\*\*\*\*\*\*\*...
  - MT LLVSVSGTAAAFMPTFPLYCLFRFLLASAVAGVMMNTAS

HP LGLLAVMEWTAARARPLVMTLNSLGFSFGHGLTAAVAYGVRDWTLLQLVVSVPFFLCFLY
.\*\*\*\*.\*...\*\*\*\*\*\*\*. \*\*...\*\*\*\*\*\*.\*. \* . \*\*\*...\*...\*\*...\* . \*\*\*...\*...\*\*

- MT ----LLMEWTSAQGSPLVMTLNALGFSFGQVLTGSVAYGVRSWRMLQLAVSAPFFLFFVY
- 25 HP SWWLAESARWLLTTGRLDWGLQELWRVAAINGKGAVQDTLTPEVLLSAMREELSMGQPPA

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI792236). However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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## <HP03700> (SEQ ID NOS: 2, 12, and 22)

Determination of the whole base sequence of the cDNA insert of clone HP03700 obtained from cDNA library of human kidney revealed the structure consisting of a 45-bp 5'-untranslated region, a 732-bp ORF, and a 2546-bp 3'untranslated region. The ORF encodes a protein consisting of 243 amino acid residues and there existed three putative 2 depicts domains. Figure transmembrane hydrophobicity/hydrophilicity profile, obtained by the Kytethe present protein. of Doolittle method, translation resulted in formation of a translation product of 27 kDa that was somewhat larger than the molecular weight of 25,561 predicted from the ORF.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to mouse yolk sac permease-like molecule 1 (Accession No. AAA92292). Table 3 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and mouse yolk sac permease-like molecule 1 (MY). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 74.5% in the N-terminal region of 231 amino acid residues.

Table 3

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20 HP SGGVWGD

MY LGSCQIPLCSWRPSSTSTHICIPVFRLLSVLAPVACVWFISAFVGTSVIPLQLSEPSDAP

The search of the GenBank using the base sequences

of the present cDNA has revealed the registration of

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sequences that shared a homology of 90% or more (for example, Accession No. AW167520). However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03935> (SEQ ID NOS: 3, 13, and 23)

Determination of the whole base sequence of the cDNA insert of clone HP03935 obtained from cDNA library of human kidney revealed the structure consisting of a 72-bp 5'-untranslated region, a 1386-bp ORF, and a 127-bp 3'untranslated region. The ORF encodes a protein consisting of 461 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 3 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. translation resulted in formation of a translation product of 56 kDa that was somewhat larger than the molecular weight of 52,052 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 61 kDa. In addition, there exists in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Ser-Ser at position 193 and Asn-Ser-Thr at position 236). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from histidine at position 32.

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The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to Arabidopsis thaliana hypothetical protein (Accession No. CAB41318). Table 4 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and Arabidopsis thaliana hypothetical protein (AT). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 30.8% in the intermediate region of 214 amino acid residues.

15 Table 4

HP MAPOSLPSSRMAPLGMLLGLLMAACFTFCLSHQNLKEFALTNPEKSSTKETERKETKAEE

HP ELDAEVLEVFHPTHEWQALQPGQAVPAGSHVRLNLQTGEREAKLQYEDKFRNNLKGKRLD

20

AT MPTIFFFRYVFLLVVISLVGFSIAEKVNSSGGMVWSSVRDEAELVEDSGVVIGEQDQ

HP INTNTYTSQDLKSALAKFKEGAEMESSKEDKARQAEVKRLFRPIEELKKDFDELNVVIET

. \*.... .\* .. . . \* .. \*\*\*. ..\*. . .

25 AT IDGGFSSLDGMLHWAIGHSDPATLKEAAKDAEKMS-LDELQKRQLELKELVEKLK--MPS

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<i>:</i>	HP	${\tt DMQIMVRLINKFNSSSSSLEEKIAALFDLEYYVHQMDNAQDLLSFGGLQVVINGLNSTEP}$
	•	* * *. ** ***. ** * ***. ** . ***. ** **
	AT	${\tt NAKLMQIAIDDLNNSSLSLEDRHRALQELLILVEPIDNANDLSKSGGLRVVAGELNHDDT}$
5		
	HP	$\verb LVKEYAAFVLGAAFSSNPKVQVEAIEGGALQKLLVILATEQPLTAKKKVLFALCSLLRHF $
		* **. *** * . ** ** * *** . * *. *
	AT	EVRKLAAWVLGKASQNNPFVQEQVLELGALTT-LIKMVNSSSTEEAVKALFAVSALIRNN
10	HP	PYAQRQFLKLGGLQVLRTLVQEKGTEV-LAVRVVTLLYDLVTEKMFAEEEAELTQEMSPE
,		.* *. * .** ** *. *****
	AT	IAGQDLFFAAHGYIMLRDVMNNGSLDMKLRRKAVFLVGDLAESQLQNTEKDELPIFKDRL
	НР	${\tt KLQQYRQVHLLPGLWEQGWCEITAHLLALPEHDAREKVLQTLGVLLTTCRDRYRQDPQLG}$
15		
	AT	FLKSVVDLIVVLDLDLQEKALTAIQTLLQLKSIEPQVLKESCGLEEALERMKLQLEESMA
	НР	RTLASLQAEYQVLASLELQDGEDEGYFQELLGSVNSLLKELR
20	ΑT	DEYKRDYAADVESIRGEVELIFRQKLGLL

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AW025017) among ESTs. However, since they are

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partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10755> (SEQ ID NOS: 4, 14, and 24)

Determination of the whole base sequence of the cDNA insert of clone HP10755 obtained from cDNA library of human kidney revealed the structure consisting of a 55-bp 5'-untranslated region, a 1944-bp ORF, and a 123-bp 3'-untranslated region. The ORF encodes a protein consisting of 647 amino acid residues and there existed eight putative transmembrane domains. Figure 4 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human hypothetical protein KIAA0062 (Accession No. BAA06685). Table 5 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human hypothetical protein KIAA0062 (KI). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention,

respectively. The both proteins shared a homology of 30.6% in the C-terminal region of 408 amino acid residues.

Table 5

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- HP MASLYSLELGLLLAVLVVTATASPPAGLLSLLTSGQGALDQEALGGLLNTLADRVHCTNG
- HP PCGKCLSVEDALGLGEPEGSGLPPGPVLEARYVARLSAAAVLYLSNPEGTCEDTRAGLWA
- 10 HP SHADHLLALLESPKALTPGLSWLLQRMQARAAGQTPKTACVDIPQLLEEAVGAGAPGSAG
  - KI RVYADAPAKLLLPPPAAWDLAVRLRGAEAASERQVYSVTM
  - HP GVLAALLDHVRSGSCFHALPSPQYFVDFVFQQHSSEVPMTLAELSALMQRLGVGREAHSD

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- KI KLLLLHPAFQSCLLLTLLGLWRTTPEAHASSLGAPAISAASFLQDLIHRYGEGDSLTLQQ
- HP HSHRHRGASSRDPVPLISSSNSSSVWDTVCLSARDVMAAYGLSEQAGVTPEAWAQLSPAL
- 20 KI LKALLNHLDVGVGRGNVTQHVQGHRNLSTCFSSGDLFTAHNFSEQSRIGSSELQEFCPTI
  - HP LQQQLSGACTSQSRPPVQDQLSQSER----YLYGSLATLLICLCAVFGLLLLTCTGCR
  - KI LQQLDSRACTSENQENEENEQTEEGRPSAVEVWGYGLLCVTVISLCSLLGASVVPFMK-K

	HP GVAHYILQTFLSLAVGALTGDAVLHLTPKVLGLHTHSEEGLSPQPTWRLLAMLAGLYAFF
	* *. **. * *
	KI TFYKRLLLYFIALAIGTLYSNALFQLIPEAFGFNPL-EDYYVSKSAVVFGGFYLFF
	·
5	HP LFENLFNLLL-PRDPEDLEDGPCGHSS-HSHGGHSHGVSLQLAPSELRQPKPPHEG
	. **** .***.
	KI FTEKILKILLKQKNEHHHGHSHYASESLPSKKDQEEGVMEKLQNGDLDHMIPQHCSSELD
	HP SRADLVAEESPELLNPEPRRLS-PELRLLPYMITLGDAVHNFADGLAV
10	.,*.*.* *****.*******.
	KI GKAPMVDEKVIVGSLSVQDLQASQSACYWLKGVRYSDIGTLAWMITLSDGLHNFIDGLAI
	HP GAAFASSWKTGLATSLAVFCHELPHELGDFAALLHAGLSVRQALLLNLASALTAFAGLYV
	**, *, * *, **, *, *, *, *******. **, **,
15	KI GASFTVSVFQGISTSVAILCEEFPHELGDFVILLNAGMSIQQALFFNFLSACCCYLGLAF
	HP ALAVGVSEESEAWILAVATGLFLYVALCDMLPAMLKVRDPRPWLLFLLHNVGLLG
	* *. **.*.* *** *** ** ** **.
	KI GILAG-SHFSANWIFALAGGMFLYISLADMFPEMNEVCQEDERKGSILIPFIIQNLGLLT
20	
	HP GWTVLLLLSLYEDDITF
	*. * * *
	KI GFTIMVVLTMYSGQIQIG

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base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA42490) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10760> (SEQ ID NOS: 5, 15, and 25)

Determination of the whole base sequence of the cDNA insert of clone HP10760 obtained from cDNA library of human kidney revealed the structure consisting of a 61-bp 5'-untranslated region, a 1341-bp ORF, and a 373-bp 3'untranslated region. The ORF encodes a protein consisting of 446 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 5 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 48 kDa that was somewhat smaller than the molecular weight of 49,468 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 50 kDa. In addition, there exists in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Ala-Thr at position 144 and Asn-Ile-Ser at position 243). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal WO 01/49728 PCT/JP00/09359

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sequence, allows to expect that the mature protein starts from glutamic acid at position 27.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human 25 kDa trypsin inhibitor (Accession No. BAA25066). Table 6 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human 25 kDa trypsin inhibitor (TI). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 33.5% in the intermediate region of 185 amino acid residues.

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Table 6

HP

MLHPETSPGRGHLLAVLLALLGTAWAEVWPPQLQEQAPMAG

20 TI MIAISAVSSALLFSLLCEASTVVLLNSTDSSPPTNNFTDIEAALKAQLDSADIPKARRKR

HP ALNRKESFLLLSLHNRLRSWVQPPAADMRRLDWSDSLAQLAQARAALCGIPTPSLASGLW
.....\*. \*\*..\*. \* \*\*\*\*\*.\* . \*...\*\*. \*...\*\*
TI YISQNDMIAILDYHNQVRGKVFPPAANMEYMVWDENLAKSAEAWAATC-IWDHG-PSYLL

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- HP RTLQVGWNMQLLPAGLASFVEVVSLWFAEGQRYSHA-AGEC-----AR--NATCTHYTQL

  \* \* . . . . \* . \* . . . \* \* . . \*\*\*\*\*\*\*.

  TI RFLGQN--LSVRTGRYRSILQLVKPWYDEVKDYAFPYPQDCNPRCPMRCFGPMCTHYTQM
- 5 HP VWATSSQLGCGRHLCSAGQA--AI---EAF-VCAYSPGGNWEVNGKTIIPYKKGAWCSLC

  \*\*\*\*\*...\*\*. \* \* ..... \*\*.\*\* \* \* ... \*\*\* \* ... \* ... \*\*\* \* ... \* ... \*\*\* \* ... \*
- HP TASVSGCFKAWDHAGGLCEVPRNPCRMSCQNHGRLNISTCHCHCPPGYTGRYCQVRCSLQ

  10 ..\*.\*

## TI PPSYGGSCTDNLCFPGVTSNYLYWFK

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI792411) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10764> (SEQ ID NOS: 6, 16, and 26)

Determination of the whole base sequence of the CDNA insert of clone HP10764 obtained from cDNA library of human kidney revealed the structure consisting of a 326-bp 5'-untranslated region, a 594-bp ORF, and a 452-bp 3'-untranslated region. The ORF encodes a protein consisting of

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197 amino acid residues and there existed two putative transmembrane domains. Figure 6 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 25 kDa that was somewhat larger than the molecular weight of 21,508 predicted from the ORF.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H45965) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

15 <HP10768> (SEQ ID NOS: 7, 17, and 27)

Determination of the whole base sequence of the cDNA insert of clone HP10768 obtained from cDNA library of human kidney revealed the structure consisting of a 100-bp 5'-untranslated region, a 1623-bp ORF, and a 351-bp 3'untranslated region. The ORF encodes a protein consisting of 540 amino acid residues and there existed nine putative depicts the domains. Figure transmembrane hydrophobicity/hydrophilicity profile, obtained by the Kytethe present protein. In Doolittle method, of translation resulted in formation of a translation product of high molecular weight.

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA459236) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10769> (SEQ ID NOS: 8, 18, and 28)

Determination of the whole base sequence of the cDNA insert of clone HP10769 obtained from cDNA library of human kidney revealed the structure consisting of a 11-bp 5'-untranslated region, a 1329-bp ORF, and a 912-bp 3'untranslated region. The ORF encodes a protein consisting of 442 amino acid residues and there existed two putative transmembrane Figure 8 depicts the domains. hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 52 kDa that was somewhat larger than the molecular weight of 49,101 predicted from the ORF.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI625881) among ESTs. However, since they are

partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10784> (SEQ ID NOS: 9, 19, and 29)

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Determination of the whole base sequence of the cDNA insert of clone HP10784 obtained from cDNA library of human kidney revealed the structure consisting of a 60-bp 5'-untranslated region, a 789-bp ORF, and a 612-bp 3'-untranslated region. The ORF encodes a protein consisting of 262 amino acid residues and there existed six putative transmembrane domains. Figure 9 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 28 kDa that was almost identical with the molecular weight of 27,551 predicted from the ORF.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to rice (Oryza sativa) hypothetical protein (Accession No. AAD39600). Table 7 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and rice hypothetical protein (OS). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that

of the protein of the present invention, respectively. The both proteins shared a homology of 40.0% in the intermediate region of 195 amino acid residues.

5 Table 7

HP

MTPEDPEETQPLLGPPGGSAPRGR

OS MSFRGEESGGEDGGRTASASDLRKPFLHTGSWYKMSSAGGGGGMGSRLGSSAYSLRDSSV

- HP RVFLAAFAAALGPLSFGFALGYSSPAIPSLQRAAPPAPRLDDAAASWFGAVVTLGAAAGG
  - \* . . . \*\*\*\*. \*. \*. \*\*\*. . . . . . \*. . . \* \*\*. . . . \*\* . \*.
- OS SAVLCTLIVALGPIQFGFTCGFSSPTQDAI----ISDLGLTLSEFSLFGSLSNVGAMVGA
- 15 HP VLGGWLVDRAGRKLSLLLCSVPFVAGFAVITAAQDVWMLLGGRLLTGLACGVASLVAPVY
  - . .\* ... \*\*\* \*\*. ... \* . \*. .\*. \*. .\*. \*\*\*\*.\*. . \*\* \* \*.\*\*\*
  - OS IASGQIAEYIGRKGSLMIAAIPNIIGWLAISFAKDSSFLFMGRLLEGFGVGVISYVVPVY
  - HP ISEIAYPAVRGLLGSCVQLMVVVGILLAYLAGWVLEWRWLAVLGCVPPSLMLLLMCFMPE
- - OS IAEIAPQTMRGALGSVNQLSVTIGILLAYLLGMFVPWRILSVLGILPCSILIPGLFFIPE
  - HP TPRFLLTQHRRQEAAPGLVRCGHGVQHECLRRLLQADPGWPWQLLARGHLGACLCTAC
    - .\*\*.\* . .... \*
- OS SPRWLAKMGKMEDFESSLQVLRGFETDIAVEVNEIKRSVQSSRRRTTIRFADIKQKRYSV

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AW028826) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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<HP10786> (SEQ ID NOS: 10, 20, and 30)

Determination of the whole base sequence of the cDNA insert of clone HP10786 obtained from cDNA library of human kidney revealed the structure consisting of a 78-bp 5'-untranslated region, a 459-bp ORF, and a 585-bp 3'-untranslated region. The ORF encodes a protein consisting of 152 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 10 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 17 kDa that was almost identical with the molecular weight of 16,904 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AW052022) among ESTs.

However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03727> (SEQ ID NOS: 31, 41, and 51)

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Determination of the whole base sequence of the cDNA insert of clone HP03727 obtained from cDNA library of human kidney revealed the structure consisting of a 254-bp 5'-untranslated region, a 1008-bp ORF, and a 355-bp 3'untranslated region. The ORF encodes a protein consisting of 335 amino acid residues and there existed one putative domain. Figure 11 depicts the transmembrane hydrophobicity/hydrophilicity profile, obtained by the Kytethe present protein. of Doolittle method, translation resulted in formation of a translation product of 41 kDa that was somewhat larger than the molecular weight of 37,999 predicted from the ORF.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to protein MG87 from diabetic rat kidney (Accession No. AAC64190). Table 8 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and protein MG87 from diabetic rat kidney (RD). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue

similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 74.2% in the entire region.

## 5 Table 8

- RD MGSSSSTALARLGLPGQPRSTWLGVAALGLAAVALGTVAWRRARPRRRRQLQQVGTVSKV

- RD WIYPIKSCKGVSVCETECTDMGLRCGKVRDRFWMVVKEDGHMITARQEPRLVLVTITLEN
- - RD NYLMLEAPGMEPIVLPIKLPSSNKIHDCRLFGLDIKGRDCGDEVARWFTSYLKTQAYRLV
- - RD QFDTKMKGRTTKKLYPSESYLQNYEVAYPDCSPIHLISEASLVDLNTRLQKKVKMEYFRP
- 25 RD NIVVSGCEAFEEDTWDELLIGDVEMKRVLSCPRCVLTTVDPDTGIIDRKEPLETLKSYRL

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HP CDPSERELYKLSPLFGIYYSVEKIGSLRVGDPVYRMV

\*\*\*\* \*\* \*\*\*\*\*\*\*\*\*\*\*\*\*

RD CDPSVKSLYQSSPLFGMYFSVEKIGSLRVGDPVYRMVD

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI912794) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03801> (SEQ ID NOS: 32, 42, and 52)

Determination of the whole base sequence of the CDNA insert of clone HP03801 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 158-bp 5'-untranslated region, a 627-bp ORF, and a 964-bp 3'-untranslated region. The ORF encodes a protein consisting of 208 amino acid residues and there existed six putative transmembrane domains. Figure 12 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 23 kDa that was almost identical with the molecular weight of 22,526 predicted from the ORF.

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The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human hypothetical protein CGI-15 (Accession No. AAD27724). Table 9 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human hypothetical protein CGI-15 (CP). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The amino acid sequences of the two proteins were completely different each other in the N-terminal, intermediate and C-terminal regions although partial match was observed.

## 15 Table 9

- CP VLFILIFSLIFKLEELRAALVLVVLLIAGGLFMFTYKSTQFNVEGFAWCWGPRSSVAFAG
- CP PSPRCSCRRLNSASRIPSTPCSTCSHSCSWGLFPLFAVFEGLHLSTSEKIFRFQDTGLLL
- 25 HP RVLGSLFLGGILAFGLGFSEFLLVSRTSSLTLSIAGIFKEVCTLLLAAHLLGDQISLLNW

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- CP RVLGSLFLGGILAFGLGFSEFLLVSRTSSLTLSIAGIFKEVCTLLLAAHLLGDQISLLNW
- HP LGFALCLSGISLHVALKALHSRGNPESLPEASVFCSSPCDS
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CP LGFASASREYPSTLPSKPCIPEVMVAPRP

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI741613) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

15 <hP03883> (SEQ ID NOS: 33, 43, and 53)

Determination of the whole base sequence of the cDNA insert of clone HP03883 obtained from cDNA library of human kidney revealed the structure consisting of a 59-bp 5'-untranslated region, a 1221-bp ORF, and a 122-bp 3'untranslated region. The ORF encodes a protein consisting of 406 amino acid residues and there existed eight putative Figure 13 depicts domains. the transmembrane hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product

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of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the choline/ethanolamine to human similar protein was phosphotransferase (Accession No. NP\_006081). Table 10 shows the comparison between amino acid sequences of the human present invention (HP) and protein of the choline/ethanolamine phosphotransferase (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 66.8% in the entire region. addition, the amino acid sequence from position 70 to position 311 of the present protein shared a homology of 98.3% with human AAPT1-like protein (Accession No. AAD44019).

Table 10

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MAAGAGAGSAPRWLRALSEPLSAAQLRRLEEHRYSAAG

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CE MSGHRSTRKRCGDSHPESPVGFGHMSTTGCVLNKLFQLPTPPLSRHQLKRLEEHRYQSAG

- CE RSLLEPLMQGYWEWLVRRVPSWIAPNLITIIGLSINICTTILLVFYCPTATEQAPLWAYI
- 5 CE ACACGLFIYQSLDAIDGKQARRTNSSSPLGELFDHGCDSLSTVFVVLGTCIAVQLGTNPD

  - CE WMFFCCFAGTFMFYCAHWQTYVSGTLRFGIIDVTEVQIFIIIMHLLAVIGGPPFWQSMIP
- HP QYFNNFIDEYVVLWMAMVISSFDMVIYFSALCLQISRHLHLNIFKTACHQAPEQVQVLSS

  \*\*\*\*. \*\*\*\*. \* \*\*... \* ... \* \*\*... \*.
  - CE QYFNSFIDEYIVLWIALVFSFFDLIRYCVSVCNQIASHLHIHVFRIKVSTAHSNHH

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example,

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Accession No. AI816449) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03913> (SEQ ID NOS: 34, 44, and 54)

Determination of the whole base sequence of the cDNA insert of clone HP03913 obtained from cDNA library of human kidney revealed the structure consisting of a 344-bp 5'-untranslated region, a 1857-bp ORF, and a 273-bp 3'untranslated region. The ORF encodes a protein consisting of 618 amino acid residues and there existed thirteen putative Figure 14 depicts domains. transmembrane hydrophobicity/hydrophilicity profile, obtained by the Kytethe present protein. In vitro Doolittle method, of translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human solute carrier family 5 (Accession No. NP\_000444). Table 11 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human solute carrier family 5 (SC). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that

of the protein of the present invention, respectively. The both proteins shared a homology of 48.3% in the entire region.

5 Table 11

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SC MEAVETGERPTFGAWDYGVFALMLLVSTGIGLWVGLARGGQRSAEDFFTGGRRLAALPVG

- HP LGGLKAVVWTDAFQMVVMIVGFLTVLIQGSTHAGGFHNVLEQSTNGSRLHIFDFDVDPLR

  20 .\*\*. \*\*\*\*\*\*\*. \*\*. \*\*. .\*\* . .\*\* . .\*\* . . \* \*\*.... \*\*.

  SC VGGMKAVVWTDVFQVVVMLSGFWVVLARGVMLVGGPRQVLTLAQNHSRINLMDFNPDPRS

	HP LIMYSHFKDCDPWTSGIISAPDQLMPYFVME1FATMPGLPGLFVACAFSGTLSTVASSIN
	**** * ***** ** .***.**.***.***
	SC IVMFVFYTDCDPLLLGRISAPDQYMPLLVLDIFEDLPGVPGLFLACAYSGTLSTASTSIN
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	HP ALATVTFEDFVKSCFPHLSDKLSTWISKGLCLLFGVMCTSMAVAASVM-GGVVQASLSIH
	*.*.** *** * *****.** ** ***.*.*
	SC AMAAVTVEDLIKPRLRSLAPRKLVIISKGLSLIYGSACLTVAALSSLLGGGVLQGSFTVM
10	HP GMCGGPMLGLFSLGIVFPFVNWKGALGGLLTGITLSFWVAIGAFIYPAPASKTWPLPLST
	***.** * *** * *.*.** .***.** .** ** *.
	SC GVISGPLLGAFILGMFLPACNTPGVLAGLGAGLALSLWVALGATLYPPSEQTMRVLPSSA
	HP DQCIKSNVTATGPPVLSSRPGIADTWYSISYLYYSAVGCLGCI
15	**.*. ** .**********.*. *
	SC ARCVALSVNASGLLDPALLPANDSSRAPSSGMDASRPALADSFYAISYLYYGALGTLTTV
	HP VAGVIISLITGRQRGEDIQPLLIRPVCNLFCFWSKKYKTLCWCGVQHDSGTEQENLENGS
	. *** .*** *
20	SC LCGALISCLTGPTKRSTLAPGLLWWDLARQTASVAPKEEVAILDDNLVKGPEELPTGNKK
	HP ARKQGAESVLQNGLRRESLVHVPGYDPKDKSYNNMAFETTHF
	SC PPGFLPTNEDRLFFLGQKELEGAGSWTPCVGHDGGRDQQETNL

C

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PCT/JP00/09359

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI733508) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

## <HP10753> (SEQ ID NOS: 35, 45, and 55)

Determination of the whole base sequence of the cDNA insert of clone HP10753 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 141-bp 5'-untranslated region, a 627-bp ORF, and a 2528-bp 3'-untranslated region. The ORF encodes a protein consisting of 208 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the inner portion. Figure 15 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product 20 of 28 kDa that was somewhat larger than the molecular weight of 21,518 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from methionine at position 32. 25

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AW162064) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10758> (SEQ ID NOS: 36, 46, and 56)

Determination of the whole base sequence of the cDNA insert of clone HP10758 obtained from cDNA library of human kidney revealed the structure consisting of a 25-bp 5'-untranslated region, a 1509-bp ORF, and a 284-bp 3'untranslated region. The ORF encodes a protein consisting of 502 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the inner portion. Figure 16 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 60 kDa that was somewhat larger than the molecular weight of 55,848 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 66 kDa. In addition, there exists in the amino acid sequence of this protein six sites at which N-glycosylation may occur (Asn-Val-Ser at position 67, Asn-Tyr-Thr at position 103, AsnWO 01/49728

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Phe-Thr at position 156, Asn-Ile-Thr at position 183, Asn-Phe-Thr at position 197 and Asn-Lys-Ser at position 283). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from alanine at position 15.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. T96740) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10771> (SEQ ID NOS: 37, 47, and 57)

Determination of the whole base sequence of the cDNA insert of clone HP10771 obtained from cDNA library of human kidney revealed the structure consisting of a 36-bp 5'-untranslated region, a 1011-bp ORF, and a 599-bp 3'-untranslated region. The ORF encodes a protein consisting of 336 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 17 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 41 kDa that was somewhat larger than the molecular weight

of 37,924 predicted from the ORF.

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The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human interferon- $\alpha$  induced protein (Accession No. AR053364). The C-terminal portion downstream from methionine at position 51 of the protein of the present invention matched with the C-terminal portion downstream from methionine at position 12 of human interferon- $\alpha$  induced protein. However, the putative transmembrane domain at the N-terminus observed for the protein of the present invention was not present in human interferon- $\alpha$  induced protein.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA452543) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10778> (SEQ ID NOS: 38, 48, and 58)

Determination of the whole base sequence of the cDNA insert of clone HP10778 obtained from cDNA library of human kidney revealed the structure consisting of a 173-bp 5'-untranslated region, a 1023-bp ORF, and a 220-bp 3'-untranslated region. The ORF encodes a protein consisting of 340 amino acid residues and there existed six putative

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transmembrane domains. Figure 18 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA429745) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10781> (SEQ ID NOS: 39, 49, and 59)

Determination of the whole base sequence of the CDNA insert of clone HP10781 obtained from cDNA library of human kidney revealed the structure consisting of a 88-bp 5'-untranslated region, a 672-bp ORF, and a 1167-bp 3'-untranslated region. The ORF encodes a protein consisting of 223 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 19 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 31 kDa that was larger than the molecular weight of 24,239 predicted from the ORF. In this case, the addition of

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a microsome led to the formation of a product of 33 kDa. In addition, there exists in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Asn-Thr at position 70 and Asn-Thr-Ser at position 71). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from gluthamine at position 23.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA334609) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10785> (SEQ ID NOS: 40, 50, and 60)

Determination of the whole base sequence of the cDNA insert of clone HP10785 obtained from cDNA library of human kidney revealed the structure consisting of a 171-bp 5'-untranslated region, a 930-bp ORF, and a 318-bp 3'-untranslated region. The ORF encodes a protein consisting of 309 amino acid residues and there existed six putative transmembrane domains. Figure 20 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro

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translation resulted in formation of a translation product of high molecular weight.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI822041) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03878> (SEQ ID NOS: 61, 71, and 81)

Determination of the whole base sequence of the cDNA insert of clone HP03878 obtained from cDNA library of human kidney revealed the structure consisting of a 77-bp 5'-untranslated region, a 1800-bp ORF, and a 139-bp 3'untranslated region. The ORF encodes a protein consisting of 599 amino acid residues and there existed ten putative Figure 21 depicts the transmembrane domains. hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to flounder (Pseudopleuronectes americanus) Na/Pi cotransport system protein (Accession No.

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AAB16821). Table 12 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and flounder Na/Pi cotransport system protein (PN). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 57.1% in the region of 545 amino acid residues other than the N-terminal and C-terminal regions.

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Table 12

HP	MPSSLPGSQVPHPTLDAVDLVEKTLRNEGTSSSAPVLEEGDTDPWTLPQLKDTSQPWKEL
	* *. ***. *. * * *. **
PN	MAPRQKVGTNSSPKPALDDDAPVGNIPPAYSTLDLVSDDPDADPWNAPELIDNGVKWSEL
HP	RVAGRLRRVAGSVLKACGLLGSLYFFICSLDVLSSAFQLLGSKVAGDIFKDNVVLSNPVA
	. ***** .*** *******************
PN	DTKGKMMRVLTGLLKLVALLGLLYFFICSLDVLSSAFQLVGGKAAGDIFKDNAVLANPVA
HP	GLVIGVLVTALVQSSSTSSSIVVSMVAAKLLTVRVSVPIIMGVNVGTSITSTLVSMAQSG
	************************************ **.* ******
PN	GLVIGVLVTVMVQSSSTSSSIVVSMVSSGLLDVQSAVPIIMGANIGTSVTNTIVAMMQAG
HP	DRDEFQRAFSGSAVHGIFNWLTVLVLLPLESATALLERLSELALGAASLTPRAQAPDILK
	**, **, ***, *, . **, . ****, **, ***** **, . * . *
PN	DRNEFRRAFAGATVHDFFNWLAVLILLPLEVATGVLYKLTHLIIESFNIQGGEDAPDLLN
HP	VLTKPLTHLIVQLDSDMI—MSSATGNATNSSLIKHWCGTTGQPT——QENSSCGAFGPC
	*, *, ***, *****, * *, * ****, ** * *
PN	VITDPLTDSIVQLDKNVISLIATNDEAAVNMSLIKEWCKTKTNVTFWNATVENCTAGALC
HP	TEKNSTAPADRLPCRHLFAGTELTDLAVGCILLAGSLLVLCGCLVLIVKLLN
	*
PN	WREGNI.TWTMLNKTWIINOERCKHIFANTTLPDLAVGLILLALSLFVLCTCLILIVKLLN

- HP SVLRGRVAQVVRTVINADFPFPLGWLGGYLAVLAGAGLTFALQSSSVFTAAVVPLMGVGV

  \*. \*. \*. \*\* \* . . \*\*\*. \*\*\*\*\* \* . . \*\*\*. \* . . \*\*\*. \* . \*\*\*
  PN SMLKGOVAVVIKRVINTDFPFPFCWVTGYIAIFVGAGMTFIVQSSSVFTSAITPLVGIGV
- HP ISLDRAYPLLLGSNIGTTTTALLAALASPADRMLSALQVALIHFFFNLAGILLWYLVPAL
- PN ISLERAYPLTLGSNIGTTTTAILAAMASPAEKLKESLQIALCHFFFNVMGILLFYPIPFT

- PN RVP I RLARGLGNHTAKYRWFAGLYLVLCFLVFPLTVFGLSMAGWQVLVGVGVPFVVL I VF
- HP VILVTVLQRRRPAWLPVRLRSWAWLPVWLHSLEPWDRLVTRCCPCNVCSPPKATTKEAYC

  \*\*. \*. \*. \* \* . \*\* \*... \*\* \*\*\* . \*\*
- PN VIVVNVMQSRCPRFLPKVLQDWDFLPRPLHSMAPWDTVVTSALGFCGKYCCCCKCCKKT
- HP YENPEILASQQL
- PN EDENMKNNTKSLEMYDNPSMLKDEDTKEASKATHL

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI792826) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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<HP03884> (SEQ ID NOS: 62, 72, and 82)

Determination of the whole base sequence of the cDNA insert of clone HP03884 obtained from cDNA library of human kidney revealed the structure consisting of a 336-bp 5'-untranslated region, a 246-bp ORF, and a 864-bp 3'untranslated region. The ORF encodes a protein consisting of 81 amino acid residues and there existed one putative Figure 22 depicts the domain. transmembrane hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa that was almost identical with the molecular weight of 8,928 predicted from the ORF.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to rat cortexin (Accession No. P41237). Table 13 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and rat

cortexin (RC). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 47.9% in the entire region.

## Table 13

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- - RC MSAPWTLSPEPLPPSTGPPVGAGLDVEQRTVFAFVLCLLVVLVLLMVRCVRILLDPYSRM
  - HP PTSTWADGLEGLEKGQFDHALA
    - \*. \*. \*. \* \*. \*\*. \*\*\*\* \*\*
- RC PASSWTDHKEALERGQFDYALV

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI791379) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03934> (SEQ ID NOS: 63, 73, and 83)

25 Determination of the whole base sequence of the

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cDNA insert of clone HP03934 obtained from cDNA library of human kidney revealed the structure consisting of a 39-bp 5'-untranslated region, a 1965-bp ORF, and a 463-bp 3'-untranslated region. The ORF encodes a protein consisting of 654 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 23 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 80 kDa that was larger than the molecular weight of 74,110 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from arginine at position 28.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human  $\beta$ -galactosidase (Accession No. AAC12775). Table 14 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human  $\beta$ -galactosidase (BG). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 54.6% in the entire region.

Table 14

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IP, M	APKKLSCLRSLLLPLSLTLLLPQADTRSFVVDRGHDRFLLDGAPFRYVSGSLHY . * * * * * * * * * * . * . * . * * * *
3G	MPGFLVRILLLLVLLLLGPTRGLRNATQRMFEIDYSRDSFLKDGQPFRYISGSIHY
	RVPRVLWADRLIKMRWSGLNAIQFYVPWNYHEPQPGVYNFNGSRDLIAFINEAALANLL  **** * ******* ****** ***** ** *. *.
,	VILRPGPYICAEWEMGGLPSWLLRKPEIHLRTSDPDFLAAVDSWFKVLLPKIYPWLYHNG ************************************
	GNIISIQVENEYGSYRACDFSYMRHLAGLFRALLGEKILLFTTDGPE—GLKCGSLRGLY  * .*********** **** ** ** ** ** ******
	TTVDFGPADNMTKIFTLLRKYEPHGPLVNSEYYTGWLDYWGQNHSTRSVSAVTKGLENML  *******. * **. ***. ****. ***** ***
	KLGASVNMYMFHGGTNFGYWNGADKKGRFLPITTSYDYDAPISEAGDPTPKLFALRDVIS  ****** *** ****** ****** * * ****** * *

HP	KFQEVPLGPLPPPSPKMMLGPVTLHLVGHLLAFLDLLCPRGPIHSILPMTFEAVKQDHGF
	<b>**** ******. * *** .</b> . <b>* ***** **</b>
BG	KFEKVPEGP I PPSTPKFAYGKVTLEKLKTVGAALD I LCPSGP I KSLYPLTF I QVKQHYGF
HP	MLYRTYMTHTIFEPTPFWVPNNGVHDRAYVMVDGVFQGVVERNMRÐKLFLTGKLGSKLDI
	.*****.*. * ******* ***. ***. *** .* .
BG	VLYRTTLPQDCSNPAPLSSPLNGVHDRAYVAVDGIPQGVLERNNVITLNITGKAGATLDL
НP	LVENMGRLSFGSNSSDFKGLLKPPILGQTILTQWMMFPLKIDNLVKWW-FPLQ
	********* ***** * ***. *
BG	LVENMGRVNYGAYINDFKGLVSNLTLSSNILTDWTIFPLDTEDAVRSHLGGWGHRDSGHH
HP	LPKWPYPQAP-SGPTFYSKTFPILGSVGDTFLYLPGWTKGQVWINGFNLGRYWTKQ
	* *. ** . *. * ** * *** . ******
BG	DEAWAHNSSNYTLPAFYMGNFSIPSGIPDLPQDTFIQFPGWTKGQVWINGFNLGRYWPAR
HP	GPQQTLYVPRFLLFPRGALNKITLLELEDVPLQPQVQFLDKPILNSTSTLHRTH
	*** **. ** * *. * . * * . * *. * *
BG	GPQLTLFVPQHILMTSAP-NTITVLELEWAPCSSDDPELCAVTFVDRPVIGSSVTYDHPS
HP	INSLSADTLSASEPMELSGH

BG KPVEKRLMPPPPQKNKDSWLDHV

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI907720) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03949> (SEQ ID NOS: 64, 74, and 84)

Determination of the whole base sequence of the cDNA insert of clone HP03949 obtained from cDNA library of 🙃 human kidney revealed the structure consisting of a 244-bp 5'-untranslated region, a 1173-bp ORF, and a 33-bp 3'untranslated region. The ORF encodes a protein consisting of 390 amino acid residues and there existed ten putative depicts transmembrane domains. Figure 24 the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human solute carrier family 16 (Accession No. NM\_004696). Table 15 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human solute carrier family 16

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(HS). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 98.7% in the region other than the N-terminal and C-terminal regions.

Table	15
HP	MGMDDCDSFFPGPLVAIICDILGEKTTSILGAFVVTGGYLISSWATSIPFLCVTMGLL
	* . **********************************
HS	WIGSIMSSLRFCAGPLVAIICDILGEKTTSILGAFVVTGGYLISSWATSIPFLCVTMGLL
HP	$\tt PGLGSAFLYQVAAVVTTKYFKKRLALSTAIARSGMGLTFLLAPFTKFLIDLYDWTGALIL$
	***************************************
HS	PGLGSAFLYQVAAVVTTKYFKKRLALSTAIARSGMGLTFLLAPFTKFLIDLYDWTGALIL
HP	FGAIALNLVPSSMLLRPIHIKSENNSGIKDKGSSLSAHGPEAHATETHCHETEESTIKDS
	***********************
HS	${\tt FGAIALNLVPSSMLLRPIHIKSENNSGIKDKGSSLSAHGPEAHATETHCHETEESTIKDS}$
НР	TTQKAGLPSKNLTVSQNQSEEFYNGPNRNRLLLKSDEESDKVISWSCKQLFDISLFRNPF
	***************************************
HS	TTQKAGLPSKNLTVSQNQSEEFYNGPNRNRLLLKSDEESDKVISWSCKQLFDISLFRNPF
НР	FYIFTWSFLLSQLAYFIPTFHLVARAKTLGIDINDASYLVSVAGILETVSQIISGWVADQ
	**************************************
HS	FYIFTWSFLLSQLAYFIPTFHLVARAKTLGIDIMDASYLVSVAGILETVSQIISGWYADQ
HP	NWIKKYHYHKSYLILCGITNLLAPLATTFPLLMTYTICFAIFAGGYLALILPVLVDLCRN
ш	WHIRE INTEREST LICE INCLEASE AND INTEREST AND INTEREST AND INCLEASE AN
nc	NWINNWINGOVI TI GOIGHT I AD A GOOD I LIGHTS OF A TO A GOVE AT A DAY YOU CON
HS	NWIKKYHYHKSYLILCGITNLLAPLATTFPLLMTYTICFAIFAGGYLALILPVLVDLCRN
HP	STVNRFLGLASFFAGMAVLSGPPIAGNTFTTF
	<b>*********************</b> .
HS	STVNRFLGLASFFAGMAVLSGPPIAGWLYDYTQTYNGSFYFSGICYLLSSVSFFFVPLAE

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AW239415) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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<HP03959> (SEQ ID NOS: 65, 75, and 85)

Determination of the whole base sequence of the cDNA insert of clone HP03959 obtained from cDNA library of human kidney revealed the structure consisting of a 7-bp 5'untranslated region, a 1359-bp ORF, and a 531-bp 3'untranslated region. The ORF encodes a protein consisting of 452 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 25 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 53 kDa that was somewhat larger than the molecular weight of 50,798 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 55 kDa. In addition, there exists in the amino acid sequence of this protein three sites at which N-glycosylation may occur (Asn-Phe-Ser at position 64, Asn-Gly-Ser at position 126 and Asn-Val-Thr at position 362). Application of the (-3,-1) rule, a

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method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from alanine at position 27.

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The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to Arabidopsis thaliana putative carboxypeptidase (Accession No. AAD21510). Table 16 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and Arabidopsis thaliana putative carboxypeptidase (AC). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 44.3% in the region of 323 amino acid residues other than the N-terminal and C-terminal regions.

Table	
	MELALRRSPVPRWLLLLPLLLGLNAGAVIDWPTEEGKEVWDYVTVRKDAYMFWWLYYATN
AC	MDPKLGDTSKLDQHTCFGG11KV
HP	SCKNFSELPLVMWLQGGPGGSSTGFGNFEEIGPLDSDLKPRKTTWLQAASLLFVDNPVGT
	*. *. * *. ***. *. **** **** ***. *.
AC	${\tt HIELKILPSHGLSSSGSKGASGVGIGNFQEVGPLDTFLKPRNSTWLKKADLLFVDSPVGA}$
HP	GFSYVNGS—GAYAKDLAMVASDMMVLLKTFFSCHKEFQTVPFYIFSESYGGKMAAGIGL
	*. *. *. * *. * * *
. AC	${\tt GYSFVEGNQKDLYVKSDEEAAQDLTKLLQQLFNKNQTLNQSPLFIVAESYGGKIAVKLGL}$
НР	ELYKA I QRGT I KCNFAGVALGDSW I SPVDSVLSWGPYLYSMSLLEDKGLAEVSKVAEQVL
	+, +, +, . + ++ +++++++ + +, ++++ + + +, +, +, ++, ++,
AC	SVIDAVQSGKLKLHLGGVILGDSWISPEDFVFSWGPLLKHVSRLDDNGLDSSNSLAEKIK
HP	NAVNKGLYREATELWGKAEMI IEQNTDGVNFYN-ILTKSTPTSTMESSLEFTQSHLV
	* * . **. * . * . *. *. *. *** . *
AC	TQIKNGEYVGATQTWMDLENLISSKSNFVDFYNFLLDTGMDPVSLTTSLKIKKEEKIKKY
HP	CLCQ-RHVRHLQRDALSQLMNGPIRKKLKIIPEDQSWGGQATNVFVNMEEDFMKPV
	. * . *
AC	SRYLNDMRSLSDVEDVEGDLDKLMNGVIKKKLKI IPNDLIWGNNSDDVFTAMEAAFMKPV
HP	ISIVDELLEAGINVTVYNGQLDLIVDTMGQEAWVRKLKWPELPKFSQLKWKALYSDPKSL
	*. ******,.**.******.* . * * ****.**.
AC	I EDVDELLATGVDVT I YNGOLDV I CSTSGTEAWVHKLR

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. T59065) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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<HP03983> (SEQ ID NOS: 66, 76, and 86)

Determination of the whole base sequence of the cDNA insert of clone HP03983 obtained from cDNA library of human kidney revealed the structure consisting of a 42-bp 5'-untranslated region, a 1473-bp ORF, and a 341-bp 3'-untranslated region. The ORF encodes a protein consisting of 490 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 26 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glutamic acid at position 22.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human ClqR protein (Accession No. AAB53110). Table 17 shows the comparison between amino acid

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sequences of the human protein of the present invention (HP) and human ClqR protein (HC). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 25.8% in the N-terminal region of 310 amino acid residues. Since the positions of 17 cysteine residues are conserved, in particular, the two proteins are considered to assume similar higher-order structures.

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Table 17

HP	MRPAFALCLLWQALWPGPGGGEHPTADRAGCSASGACYSLHHATMKRQAAEEACILRGG
	* * **
HC	MATSMGLLLLLLLLTQPGAGTGADTEAVVC-VGTACYTAHSGKLSAAEAQNHCNQNGGI
HP	LSTVRAGAELRAVLALLRAGPGPGGGSKDLLFWVALERRRSHCTLENEPLRGFSWLSS
	*. ** * . * ** * * **. * * *
HC	LATYKSKEEAQHVQRVLAQLLRREAALTARMSKFWIGLQREKGKCLDPSLPLKGFSWV-
HP	DPGGLESDTLQWVEEPQRSCTARRC—AVLQATGGVEP—AGWKEMRC—HLRAN ** * . * * * *
HC	-GGGEDTPYSNWHKELRNSCISKRCVSLLLDLSQPLLPNRLPKWSEGPCGSPGSPGSNIE
HP	GYLCKYQFEVLCPAPRPGAASNLSYRAPFQLHSAALDFSPPGTEVSALCRGQLPIS
	***. * * * * * *
HC	GFVCKFSFKGMCRPLALGGPGQVTYTTPFQTTSSSLEAVPFASAANVACGEGDKDETQSH
HP	VTCIADEIGA-RWDKLSGDVLCPCPGRYLRAGKCAELPNCLD-DLGGFACECATGFE
	* * * *
HC	YFLCKEKAPDVFDWGSSGPLCVSPKYGCNFNNGGCHQDCFEGGDGSFLCGCRPGFR

- HP LGKDGRSCVTSGEGQPTLGGTGVPTRRPPATATSPVPQRTWPIRVDEKLGETPLVPEQDN

  \* . \* . \*.
  - ${\tt HC-LLDDLVTCASRNPCSSSPCRGGATCVLGPHGKNYTCRCPQGYQLDSSQLDCVDVDECQDS}$
  - $HP \quad SVTSIPEIPRWGSQSTMSTLQMSLQAESKATITPSGSVISKFNSTTSSATPQAFDSSSAV$
  - HC PCAQECVNTPGGFRCECWVGYEPGGPGEGACQDVDECALGRSPCAQGCTNTDGSFHCSCE
  - $HP \quad VFIFVSTAVVVLVILTMTVLGLVKLCFHESPSSQPRKESMGPPGLESDPEPAALGSSSAH$
  - HC EGYVLAGEDGTQCQDVDECVGPGGPLCDSLCFNTQGSFHCGCLPGWVLAPNGVSCTMGPV
  - HP CTNNGVKVGDCDLRDRAEGALLAESPLGSSDA
  - HC SLGPPSGPPDEEDKGEKEGSTVPRAATASPTRGPEGTPKATPTTSRPSLSSDAPITSAPL

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R51653) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10745> (SEQ ID NOS: 67, 77, and 87)

Determination of the whole base sequence of the cDNA insert of clone HP10745 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 261-bp 5'-untranslated region, a 1179-bp ORF, and a 733-bp 3'-untranslated region. The ORF encodes a protein consisting of 392 amino acid residues and there existed nine putative transmembrane domains. Figure 27 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R59881) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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Determination of the whole base sequence of the cDNA insert of clone HP10775 obtained from cDNA library of human kidney revealed the structure consisting of a 30-bp 5'-untranslated region, a 1617-bp ORF, and a 287-bp 3'-untranslated region. The ORF encodes a protein consisting of 538 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 28 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 66 kDa that was larger than the molecular weight of 55,133 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from serine at position 23.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA366320) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10782> (SEQ ID NOS: 69, 79, and 89)

Determination of the whole base sequence of the cDNA insert of clone HP10782 obtained from cDNA library of

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human kidney revealed the structure consisting of a 70-bp 5'-untranslated region, a 309-bp ORF, and a 1501-bp 3'-untranslated region. The ORF encodes a protein consisting of 102 amino acid residues and there existed three putative transmembrane domains. Figure 29 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein.

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI815463) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10787> (SEQ ID NOS: 70, 80, and 90)

Determination of the whole base sequence of the cDNA insert of clone HP10787 obtained from cDNA library of human kidney revealed the structure consisting of a 54-bp 5'-untranslated region, a 1329-bp ORF, and a 912-bp 3'-untranslated region. The ORF encodes a protein consisting of 442 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 30 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product

of 50 kDa that was almost identical with the molecular weight of 50,562 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 56 kDa. In addition, there exists in the amino acid sequence of this protein four sites at which N-glycosylation may occur (Asn-Leu-Thr at position 83, Asn-Phe-Thr at position 89, Asn-Ala-Ser at position 113 and Asn-Lys-Ser at position 151).

acid sequence of the present protein revealed that the protein was similar to rat PV-1 (Accession No. AAD41524).

Table 18 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and rat PV-1 (RP). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 61.1% in the entire region.

_	le 18
HP	MGLAMEHGGSYARAGGSSRGCWYYLRYFFLFVSLIQFLIILGLVLFMVYGNVHVSTESNL ***. *. *. *. *. ********************
ממ	MGLSMDR-SPYSRTGDRDRGCWYYLRYFFLFVSLIQFLIILGLVLFMIYGNVHATTESSL
RP	WATPWAK-25.12K1AANAACM11FK11.Ft.42F141.F11F9F4F1F11191411W11F92F
HP	QATERRAEGLYSQLLGLTASQSNLTKELNFTTRAKDAIMQMWLNARRDLDRINASFRQCQ
	. *** ** **** **. *. **. *. ** * . ** ** * ** ******
RP	RATEIRADNLYSQVVGLSAAQANLSKQLNISTLVKDTVMQQLLTTRREVERINASFRQCQ
HP	GDRVIYTNNQRYMAAIILSEKQCRDQFKDMNKSCDALLFMLNQKVKTLEVEIAKEKTICT
	** *. * . * ********** *. **. *.
RP	GDLITYINYNRFIAAIILSEKQCQEQLKEGNKTCEALLFKLGEKVKTLEMEVVKEKAVCS
нр	KDKESVLLNKRVAEEQLVECYKTRELQHQERQLAKEQLQKVQALCLPLDKDKFEMDLRNL
nr	***. *. * * * * * * * * * * * * * * * *
RP	KDKDSLLAGKRQAEMQQEACGKAREQQKQDQQVTEEQLRKVQSLCLPLDQEKFQADVLNV
M	IDIDDDDIADINAADINAANAANAA 1224221 42202 22 422 422 121
HP	WRDSIIPRSLDNLGYNLYHPLGSELASIRRACDHMPSLMSSKVEELARSLRADIERVARE
	****. *****. **. * . * . * . * . * . *
RP	WRDSLVYRSLDNIGYH-Y-SLMPEFSSLRRTCESLPGIMTTKVEELARGLRAGIERVTRE
HP	NSDLQRQKLEAQQGLRASQEAKQKVEKEAQAREAKLQAECSRQTQLALEEKAVLRKERDN
	**, ***** ** ******* **. ******
RP	NGELRRQKLELERAIQGEREARTRAGTEAQARETQLRTECARQTQLALEEKAALRTQRDD
tro	TAKINI DDUWANA NATI ATINGAT DEGITETUR (ADMINISTRATION DA CI EU
HP	
<b></b>	*****
RP	LERQLEARKRELEQLRTEYDVRISALDTCVKAKSLPAIQ-PRLPGPPPNPPPIDPASLEE

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## HP FKRKILESQRPPAGIPVAPSSG \*\*. \*\*\*\*\*\*\* \*. \*. \*\*

## RP FKKRILESQRPPLVNPAVPPSG

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base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AL041217) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03977> (SEQ ID NOS: 91, 101, and 111)

Determination of the whole base sequence of the CDNA insert of clone HP03977 obtained from cDNA library of human kidney revealed the structure consisting of a 35-bp 5'-untranslated region, a 684-bp ORF, and a 1175-bp 3'-untranslated region. The ORF encodes a protein consisting of 227 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 31 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 29 kDa that was larger than the molecular weight of 25,926 predicted from the ORF. Application of the (-3,-1)

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rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from leucine at position 30.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human gp25L2 (Accession No. CAA62380). Table 19 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human gp25L2 (GP). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 78.5% in the region other than the N-terminal region.

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Table 19 .

HP	MAGYGAGPLRAMGRQALLLLALCATGAQGLYFHIGETEKRCFIEEIPDETMVIGNYRTQM
	* **, * * . * **********************
GP	MRTLLLVLWLATRGS-ALYFHIGETEKKCFIEEIPDETMVIGNYRTQL
HP	WDKQKEVFLPSTPGLGMHVEVKDPDGKVVLSRQYGSEGRFTFTSHTPGDHQICLHSNSTR
	. ***. * . *. ***. ** ****** **. *. *
GP	YDKQREEYQPATPGFGMCVEVKDPEDKVILAREYGSEGRFTFTSHTPGEHQICLHSNSTK
HP	MALF AGGKLRYHLD I QYGEHANNYPE I AAKDKLTELQLRARQLLDQYEQ I QKEQDYQRYR
	******, **************, *. **, *****, ****, *** ********
GP	FSLFAGGMLRVHLDIQVGEHANDYAEIPAKDKLSELQLRVRQLVEQVEQIQKEQNYQRWR
HP	EERFRLTSESTNQRVLWWSIAQTVILILTGIWQMRHLKSFFEAKKLV
	***** ********* **. ** *. **********
CD	REDEPOTSESTNORVI WWS II OTI II VA I CVWOMRHI K SFFEAKKI.V

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AR052481, U.S. Patent No. 5831052) in patent data. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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<HP10649> (SEQ ID NOS: 92, 102, and 112)

Determination of the whole base sequence of the cDNA insert of clone HP10649 obtained from cDNA library of thuman epidermoid carcinoma cell line KB revealed the structure consisting of a 114-bp 5'-untranslated region, a 1059-bp ORF, and a 1240-bp 3'-untranslated region. The ORF encodes a protein consisting of 352 amino acid residues and there existed one putative transmembrane domain. Figure 32 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was almost identical with the molecular weight of 39,774 predicted from the ORF.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to Epiphyas postvittana nucleopolyhedrovirus apoptosis inhibitor iap-1 (Accession No. AAD19698). Table 20 shows the comparison between amino

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acid sequences of the human protein of the present invention (HP) and Epiphyas postvittana nucleopolyhedrovirus apoptosis inhibitor iap-1 (EP). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 40.8% in the C-terminal region of 49 amino acid residues.

Table 20

HP MESGGRPSLCQFILLGTTSVVTAALYSVYRQKARVSQELKGAKKVHLGEDLKSILSEAPG HP KCYPYAVIEGAVRSVKETLNSQFVENCKGVIQRLTLQEHKMVWNRTTHLWNDCSKIIHQR MSATSPLYI INVCENAHEVSAEHVFNVL I ERHNSFENYP I DNVAFVNSL I INGF EP HP TNTVPFDLVPHEDGVDVAVRVLKPLDSVDLGLETVYEKFHPSIQSFTDVIGHYISGERPK EP RYQNYDDAVMCEYCSAVIKNWHEDDCVEFVHATLSPYCVYANKIAQNENFANNLSTNAFL HP GIQETEEMLKVGATLTGVGELVLDNNSVRLQPPKQGMQYYLSSQDFDSLLQRQESSVKLW EP VTPGKPICVYSRLTHTNARKSTFEDYWPAALQHLVANISEAGMFHTKLGDETACFFCDCR HP KVLALVFGFATCATLFFILRKQYLQRQERLRLKQMQEEFQEHEAQLLSRAKPEDRESLKS EP VRDWLPNDDPWQRHAIANPQCYFVVCIKGDEFCNAVRQRDELAPLQSVVALEHVSNDENM HP ACVVCLSSFKSCVFLECGHVCSCTECYRALPEPKKCPICRQAITRVIPLYNS \* , \*\*, . . . \*, \* \* \* \* . \*\* \*\* . . \*\*\*. \* . . . EP ECKICLERQRDTVLLPCRHFCVCMQCYFAL-DNKCPTCRQDVTDFVKIFVV

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. T50032) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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<HP10779> (SEQ ID NOS: 93, 103, and 113)

Determination of the whole base sequence of the cDNA insert of clone HP10779 obtained from cDNA library of human kidney revealed the structure consisting of a 34-bp 5'-untranslated region, a 393-bp ORF, and a 1949-bp 3'-untranslated region. The ORF encodes a protein consisting of 130 amino acid residues and there existed two putative transmembrane domains. Figure 33 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AL042495) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention. In addition, this gene was mapped on chromosome 9q34 (Accession No. AC001644).

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<HP10790> (SEQ ID NOS: 94, 104, and 114)

Determination of the whole base sequence of the cDNA insert of clone HP10790 obtained from cDNA library of human kidney revealed the structure consisting of a 109-bp 5'-untranslated region, a 993-bp ORF, and a 53-bp 3'untranslated region. The ORF encodes a protein consisting of 330 amino acid residues and there existed one putative transmembrane domain. Figure 34 depicts hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 34 kDa that was smaller than the molecular weight of 36,642 predicted from the ORF.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AW241940) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10793> (SEQ ID NOS: 95, 105, and 115)

Determination of the whole base sequence of the cDNA insert of clone HP10793 obtained from cDNA library of human kidney revealed the structure consisting of a 70-bp 5'-untranslated region, a 1053-bp ORF, and a 206-bp 3'-

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untranslated region. The ORF encodes a protein consisting of 350 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the inner portion. Figure 35 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was somewhat larger than the molecular weight of 37,134 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 25.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA326569) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10794> (SEQ ID NOS: 96, 106, and 116)

Determination of the whole base sequence of the cDNA insert of clone HP10794 obtained from cDNA library of human kidney revealed the structure consisting of a 146-bp 5'-untranslated region, a 342-bp ORF, and a 899-bp 3'-untranslated region. The ORF encodes a protein consisting of

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113 amino acid residues and there existed one putative transmembrane domain. Figure 36 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 14 kDa that was almost identical with the molecular weight of 12,017 predicted from the ORF.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI346561) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

15 <HP10797> (SEQ ID NOS: 97, 107, and 117)

Determination of the whole base sequence of the cDNA insert of clone HP10797 obtained from cDNA library of human kidney revealed the structure consisting of a 129-bp 5'-untranslated region, a 570-bp ORF, and a 459-bp 3'-untranslated region. The ORF encodes a protein consisting of 189 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 37 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product

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of 22 kDa that was almost identical with the molecular weight of 21,053 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glutamine at position 23.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA356938) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention. In addition, this gene was mapped on chromosome 4 (Accession No. AC004067).

<HP10798> (SEQ ID NOS: 98, 108, and 118)

Determination of the whole base sequence of the cDNA insert of clone HP10798 obtained from cDNA library of human kidney revealed the structure consisting of a 25-bp 5'-untranslated region, a 834-bp ORF, and a 247-bp 3'untranslated region. The ORF encodes a protein consisting of 277 amino acid residues and there existed seven putative domains. Figure 38 depicts the transmembrane hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 27 kDa that was smaller than the molecular weight of

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30,685 predicted from the ORF.

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H92084) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10800> (SEQ ID NOS: 99, 109, and 119)

10 Determination of the whole base sequence of the cDNA insert of clone HP10800 obtained from cDNA library of human kidney revealed the structure consisting of a 158-bp 5'-untranslated region, a 825-bp ORF, and a 924-bp 3'untranslated region. The ORF encodes a protein consisting of 274 amino acid residues and there existed one putative 15 transmembrane domain. Figure 39 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product 20 of 33 kDa that was somewhat larger than the molecular weight of 31,108 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 45 kDa. In addition, there exists in the amino acid sequence of this protein five sites at which N-glycosylation may occur (Asn-25 Ile-Thr at position 145, Asn-Ile-Thr at position 151, Asn-

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Ile-Thr at position 164, Asn-Ile-Thr at position 183, and Asn-Thr-Thr at position 256).

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA729308) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

10 <HP10801> (SEQ ID NOS: 100, 110, and 120)

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Determination of the whole base sequence of the cDNA insert of clone HP10801 obtained from cDNA library of human kidney revealed the structure consisting of a 133-bp 5'-untranslated region, a 1173-bp ORF, and a 510-bp 3'-untranslated region. The ORF encodes a protein consisting of 390 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the inner portion. Figure 40 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation with the addition of microsome resulted in formation of a product of 50 kDa that was larger than the molecular weight of 41,097 predicted from the ORF. In addition, there exists in the amino acid sequence of this protein five sites at which N-glycosylation may occur (Asn-

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Leu-Ser at position 108, Asn-Val-Thr at position 169, Asn-Leu-Ser at position 213, Asn-Val-Thr at position 236 and Asn-Gly-Thr at position 307). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glutamine at position 30.

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The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human A33 antigen (Accession No. NP\_005805). Table 21 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human A33 antigen (HA). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 28.7% in the intermediate region of 265 amino acod residues.

Table 21

HP	MISLPGPLVTNLLRFLFLGLSALAPPSRAQLQLHLPANRLQAVEGGEVVLPAWY-TLHGE
	* *.* .* .* . * . *
HA	MVGKMWPVLWTLCAVRVTVDAISVETPQDVLRASQGKSVTLPCTYHTSTSS
HP	VSSSQPWEVPFVMWFFKQKEKEDQVLSYINGVTTSKPGVSLVYSMPSRNLSLRLEGLQEK
HA	REGLIQWDKLLLTHTERVVIWPFSNKNYIHG-ELYKNRVSISNNAEQSDASITIDQLTMA
HP	DSGPYSCSVNVQDKQGKSRGHSIKTLELNVLVPPAPPSCRLQGVPHVGANVTLSCQSPRS
	*. *. *. **** * * *****. *.
HA	DNGTYECSVSLMSDLEGNTKSRVRLLVLVPPSKPECGIEGETIIGNNIQLTCQSKEG
HP	KPAVQYQWDRQLPSFQTFFAPALDVIRGSLSLTNLSSSMAGVYVCKAHNEVGTAQCNVTL
	. *. ** *. * * * * * *. * . * **. **. **. **.
HA	SPTPQYSWKR-YNILNQEQPLAQPASGQPVSLKNISTDTSGYYICTSSNEEGTQFCNITV
HP	EV-STGPGAAVVAGAVVGTLVGLGLLAGLVLLYHCRGKALEEPANDIKEDAIAPRTLPWP
•	. * * * . * . *
HA	AVRSPSMNVALYVGIAVGVVAALIIIGIIIYCCCCRGKDDNTEDKEDARPNREAYEE
НР	KSSDT I SKNGTLSSVTSARALRPPHGPPRPGALTPTPSLSSQALPSPRLPTTDGAHPQP I
HA	PPEQLRELSREREEEDDYRQEEQRSTGRESPDHLDQ

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R33685) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03696> (SEQ ID NOS: 121, 131, and 141)

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Determination of the whole base sequence of the cDNA insert of clone HP03696 obtained from cDNA library of thuman umbilical cord blood revealed the structure consisting of a 184-bp 5'-untranslated region, a 1188-bp ORF, and a 589-bp 3'-untranslated region. The ORF encodes a protein consisting of 395 amino acid residues and there existed one putative transmembrane domain. Figure 41 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to rat cell surface glycoprotein GP42 (Accession No. P23505). Table 22 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and rat cell surface glycoprotein GP42 (RC). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of

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the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 46.1% in the intermediate region of amino acid residues 62-280.

Table 22

MSGMEEYTTVSGEVLQRWKIPSFKENQTLSMGAATVQSRGQYSCSGQVMYIPQTFTQTSE	HP
MLLWMVLLLC	RC
TAMVQVQELFPPPVLSAIPSPEPREGSLVTLRCQTKLHPLRSALRLLFSFHKDGHTLQDR	HP
. * ****. **** . *. *	
VSMTEAQELFQDPVLSRLNSSETSDLLLKCTTKVDPNKPASELFYSFYKDNHIIQNR	RC
GPHPELCIPGAKEGDSGLYWCEVAPEGGQVQKQSPQLEVRVQAPVSRPVLTLHHGPADPA	НР
* . **. **** * * * .**. *	
SHNPLFFISEANEENSGLYQCVYDAKDGTIQKKSDYLDIDLCTSVSQPVLTLQHEATNLA	RC
VGDMVQLLCEAQRGSPPILYSFYLDEKIVGNHSAPCGGTTSLLFPVKSEQDAGNYSCEAE	HP

\*\*, \*, . \*\*\*, \* \*\* \*\*\*\*\*\*\*, \*, . \*\*, \* . . \*\*\*, . \*\*, \* , . \*\*\*\*, \*\*

RC EGDKVKFLCETQLGSLP1LYSFYMDGE1LGEPLAPSGRAASLL1SVKAEWSGKNYSCQAE

HP NSVSRERSEPKKLSLKGSQVLFTPASNWLVPWLPAS-LLGLMVIAAALLVYVRSWRKAGP

RC NKVSRDISEPKKFPLVVSGTASMKSTT-VVIWLPVSCLVGWPWLLRF

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA446524) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03882> (SEQ ID NOS: 122, 132, and 142)

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Determination of the whole base sequence of the cDNA insert of clone HP03882 obtained from cDNA library of human kidney revealed the structure consisting of a 57-bp 5'-untranslated region, a 1653-bp ORF, and a 484-bp 3'untranslated region. The ORF encodes a protein consisting of 550 amino acid residues and there existed ten putative transmembrane domains. Figure 42 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to mouse solute carrier family 22 (cation transporter)-like protein (Accession No. NP\_033229). Table 23 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and mouse

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solute carrier family 22 (cation transporter)-like protein (MS). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 48.9% in the entire region.

Tal	ole 23
HP	${\tt MAFSKLLEQAGGVGLFQTLQVLTFILPCLMIPSQMLLENFSAAIPGHRCWTHMLDNG}$
	*******.* ** .* * * * . ******
MS	${\tt MAFPELLDRVGGLGRFQLFQTVALVTPILWVTTQNMLENFSAAVPHHRCWVPLLDNSTSQ}$
	SAVSTNMTPKALLTISIPPGPNQGPHQCRRFRQPQWQLLDPNATATSWSEADTEPCVDGW
MS	ASIPGDLGPDVLLAVSIPPGPDQQPHQCLRFRQPQWQLTESNATATWWSDAATEPCEDGW
HP	VYDRSVFTSTIVAKWDLVCSSQGLKPLSQSIFMSGILVGSFIWGLLSYRFGRKPMLSWCC
	***. *. * **** *****. **. * ***** * * **** *. *
MS	VYDHSTFRSTIVTTWDLVCNSQALRPMAQSIFLAGILVGAAVCGHASDRFGRRRVLTWSY
HP	LQLAVAGTSTIFAPTFVIYCGLRFVAAFGMAGIFLSSLTLMVEWTTTSRRAVTMTVVGCA
	* * . * * * * *
MS	LLVSVSGTAAAFMPTFPLYCLFRFLLASAVAGVMMNTASLLMEWTSAQGSPLVMTLNALG
HP	FSAGQAALGGLAFALRDWRTLQLAASVPFFAISLISWWLPESARWLIIKGKPDQALQELR
	** **. * * *. ** **** * ********
MS	FSFGQVLTGSVAYGVRSWRMLQLAVSAPFFLFFVYSWWLPESARWLITVGKLDQGLQELQ
Н	P KVARINGHK-EAKNLTIEVLMSSVKEEVASAKEPRSVLDLFCVPVLRWRSCAMLVVNFSL
	** _* _* * * **. ***. * ** *
M.	S RVAAVNRRKAEGDTLTMEVLRSAMEEEPSRDKAGASLGTLLHTPGLRHRTIISMLCWFAF
H	P_LISYYGLYFDLQSLGRDIFLLQALFGAVDFLGRATTALLLSFLGRRTIQAGSQAMAGLAI
	***. ***. **. ***. * *** **. * *** * **
1/	S CETEVOL ALDI DAL CSNIELL DAL LGIVDEPVKTGSLLL I SRLGRRLCOVSELVL PGLCI

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HP LANMLVPQDLQTLRVVFAVLGKGCFGISLTCLTIYKAELFPTPVRMTADGILHTVGRLGA

\*. \*. \*\*\*... . \*\* . . \*\*\* \*\*. \*\*. \*\*\*\* \* . . . \* \*\*

MS LSNILVPHGMGVLRSALAVLGLGCLGGAFTCITIFSSELFPTVIRMTAVGLCQVAARGGA

HP GNRQEAVTVESTSL

. ... .. \*\*.\*

MS HDTPDGSILMSTRL

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI242210) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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<HP03903> (SEQ ID NOS: 123, 133, and 143)

Determination of the whole base sequence of the cDNA insert of clone HP03903 obtained from cDNA library of human kidney revealed the structure consisting of a 108-bp 5'-untranslated region, a 657-bp ORF, and a 1988-bp 3'-untranslated region. The ORF encodes a protein consisting of 218 amino acid residues and there existed three putative

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transmembrane domains. Figure 43 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 26 kDa that was somewhat larger than the molecular weight of 23,487 predicted from the ORF.

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The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to mouse prominin (Accession No. NP\_032961). Table 24 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and mouse prominin (MP). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 27.6% in the region other than the N-terminal and C-terminal regions.

Ta!	ble 24
HP	MKHTLALLAPLLGLGLGLALSQLAAGATDCKFLGPAEHLTFTPAARARWLAPRVRAPGLL
	.* * *.* *
MP	MALVFSALLLLGLCGKISSEGQPAFHNTPGAMNYELPT-TKYETQDTFNAGIV
HP	DSLYGTVRRFLSVVQLNPFPSELVKALLNELA-SVKVNEVVRYEAGYVVCAVIAGLYL
	** *. **. *** * ** . *. * *
МР	GPLYKMVHIFLNVVQPNDFPLDLIKKLIQNKNFDISVDSKEIALYEIGVLICAILGLLFI
HP	LLVPTAGLCFCCCRCHRRCGGRVKTEHK-ALACERAALMVFLLLTTLLLLIGVVCAFVTN
	.*.*.* ** *** **** * ** ** ** ** **
МP	ILMPLVGCFFCMCRCCNKCGGEMHQRQKQNAPCRRKCLGLSLLVICLLMSLGIIYGFVAN
HP	QRTHEQMGPSIEAMPETLLSLWGLVSDVPQVSTVTPHPHVPL
	*. * * *.
MР	QQTRTRIKGTQKLAKSNFRDFQTLLTETPKQIDYVVEQYTNTKNKAFSDLDGIGSVLGGR

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI792608) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP03974> (SEQ ID NOS: 124, 134, and 144)

Determination of the whole base sequence of the cDNA insert of clone HP03974 obtained from cDNA library of human kidney revealed the structure consisting of a 41-bp 5'-untranslated region, a 1791-bp ORF, and a 253-bp 3'untranslated region. The ORF encodes a protein consisting of 596 amino acid residues and there existed twelve putative 44 transmembrane domains. Figure depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to rabbit (Oryctolagus cuniculus) sodium/glucose cotransporter protein (Accession No. AAA66065). Table 25 shows the comparison between amino acid sequences of the human protein of the present invention (HP)

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and rabbit sodium/glucose cotransporter protein (OC). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 89.1% in the entire region.

Table 25

HP	M-AANSTSDLHTPGTQLSVADIIVITVYFALNVAVGIWSSCRASRNTVNGYFLAGRDMTW
	* *. ***** *. **. ****. **. ***********
00	${\tt MVADNSTSDPHAPGPQLSVTDIVVITVYFALNVAVGIWSSCRASRNTVSGYFLAGRDMTW}$
HP	WPIGASLFASSEGSGLFIGLAGSGAAGGLAVAGFEWNATYVLLALAWVFVPIYISSEIVT
	********
OC	${\tt WPIGASLFGSSEGSGLFIGLAGSGAAGGLAVAGFDWNATYVLLALAWVFGAIYISSEIVT}$
HP	LPEYIQKRYGGQRIRMYLSVLSLLLSVFTKISLDLYAGALFYHICLGWNFYLSTILTLGI
	*. ******. ****************************
OC	LAEYIQKRFGGQRIRMYLSVLSLLLSVFTKISLDLYAGALFVHICLGWNFYLSTILTLTI
•	
HP	TALYTIAGGLAAVIYTDALQTLIMVVGAVILTIKAFDQIGGYGQLEAAYAQAIPSRTIAN
	******. ***. ******************. ****. **. ****. *****. *****. **
00	${\tt TALYTITGGLVAVIYTDALQTLIMVVGAVILAIKAFHQIDGYGQMEAAYARAIPSRTVAN}$

IP	TTCHLPRTDAMHMFRDPHTGDLPWTGMTFGLTIMATWYWCTDQVIVQRSLSARDLNHAKA
	******. ********. ********************
OC.	TTCHLPRADAMHMFRDPYTGDLPWTGMTFGLTIMATWYWCTDQVIVQRSLSARNLNHAKA
HP	GSILASYLKMLPMGLIIMPGMISRALFPDDVGCVVPSECLRACGAEVGCSNIAYPKLVME
	***************************************
0C	GSILASYLKMLPMGLMIMPGMISRALFPDEVGCVVPSECLRACGAEIGCSNIAYPKLVME
HP	LMP I GLRGLMI AVMLAALMSSLTS I FNSSSTLFTMD I WRRLRPRSGERELLLVGRLV I VA
	***, **********, . ******, ************
0C	LMPVGLRGLMIAVMMPALMSSLSSIFNSSSTLFTMDIWRRLRPCASERELLLVGRLVIV
HP	LIGYSVAWIPVLQDSNSGQLFIYMQSVTSSLAPPVTAVFVLGVFWRRANEQGAFWGLIAG
	***************************************
00	LIGVSVAWIPVLQGSNGGQLFIYMQSVTSSLAPPVTAVFTLGIFWQRANEQGAFWGLLA
HP	LVVGATRLVLEFLNPAPPCGEPDTRPAVLGSIHYLHFAVALFALSGAVVVAGSLLTPPPC
	*. ******** *. ****** ******* ******
00	LAVGATRLVLEFLHPAPPCGAADTRPAVLSQLHYLHFAVALFVLTGAVAVGGSLLTPPP
HP	SVQIENLTWWTLAQDVPLGTKAGDGQTPQKHAFWARVCGFNAILLMCVNIFFYAYFA
	. **************
00	RHQIENLTWWTLTRDLSLGAKAGDGQTPQRYTFWARVCGFNAILLMCVNIFFYAYFA

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AI793336) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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<HP03978> (SEQ ID NOS: 125, 135, and 145)

Determination of the whole base sequence of the cDNA insert of clone HP03978 obtained from cDNA library of human kidney revealed the structure consisting of a 99-bp 5'-untranslated region, a 1404-bp ORF, and a 705-bp 3'untranslated region. The ORF encodes a protein consisting of 467 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 45 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 55 kDa that was somewhat larger than the molecular weight of 52,352 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 57 kDa. In addition, there exists in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Arg-Thr at position 78 and Asn-His-Ser at position 161). Application of the (-3,-1) rule, a method for predicting the

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cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from alanine at position 22.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human tubulo-interstitial nephritis antigen (Accession No. BAA84949). Table 26 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and human tubulo-interstitial nephritis antigen (TA). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 50.0% in the region other than the N-terminal region.

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Tai	ble 26
HP	MWRCPLGLLLLLPLAGHLALGAQQGRGRRELAPGLHLRGIRDAGGRYCQEQ
	<b>*. **</b>
TA	${\tt MWTGYKILIFSYLTTEIWMEKQYLSQREVDLEAYFTRNHTVLQGTRFKRAIFQGQYCRNF}$
HP	DLCCRGRADDCALP-YLG-AICYCDLFCNRTVSDCCPDFWDFCLGVPPPFPPIQG
	. ** . *. *. * . *. **** **. * . *** ** * *
TA	G-CCEDRDDGCVTEFYAANALCYCDKFCDRENSDCCPDYKSFCREEKEWPPHTQPWYPEG
ΗР	CMHGGRIYPVLGTYWDNCNRCTCQENRQWQCDQEPCLVDPDMIKAINQGNYGWQAGNHSA
	**. ****.*** **. *.* *.
TA	CFKDGQHYEEGSVIKENCNSCTC-SGQQWKCSQHVCLVRPELIEQVNKGDYGWTAQNYSQ
HP	FWGMTLDEGIRYRLGTIRPSSSVMNMHEIYTVLNPGEVLPTAFEASEKWPNLIHEPLDQG
	******. * **** * * * * * * * * * * * * * *
TA	FWGMTLEDGFKFRLGTLPPSLMLLSMNEMTASLPATTDLPEFFVASYKWPGWTHGPLDQK
HP	NCAGSWAFSTAAVASDRVSIHSLGHMTPVLSPQNLLSCDTHQQQGCRGGRLDGAWWFLRR
,	***. ******. **. ** *. *. ******. ** ** * ***. **.
TA	NCAASWAFSTASVAADRIAIQSKGRYTANLSPQNLISCCAKNRHGCNSGSIDRAWWYLRK
HP	RGVVSDHCYPFSGRERDEAGPAPPCMMHSRAMGRGKRQATAHCPNSYVNNNDIYQVTPVY
	**. **.   ***.     . *   *   * **.   *****. ** . ***.   *   *** . * *
TA	RGLVSHACYPLFKDQNATNNGCAMASRSDGRGKRHATKPCPNNVEKSNR1YQCSPPY
HP	RLGSNDKEIMKELMENGPVQALMEVHEDFFLYKGGIYSHTPVSLGRPERYRRHGTHSVKI
	*********.*.******.*.****** **.***.*

TA RVSSNETEIMKEIMQNGPVQAIMQVHEDFFHYKTGIYRHVTSTNKESEKYRKLQTHAVKL

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HP TGWGEETLPDGRTLKYWTAANSWGPAWGERGHFRIVRGVNECDIESFVLGVWGRVGMEDM

\*\*\*\*. . . \*. \*. \*\*\*\*\*\* . \*\*\*. \*\*\*\*. . . \*

TA TGWGTLRGAQGQKEKFWIAANSWGKSWGENGYFRILRGVNESDIEKLIIAAWGQLTSSDE

HP GHH

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TA P

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R48402) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

15 <HP10735> (SEQ ID NOS: 126, 136, and 146)

Determination of the whole base sequence of the cDNA insert of clone HP10735 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 370-bp 5'-untranslated region, a 1431-bp ORF, and a 243-bp 3'-untranslated region. The ORF encodes a protein consisting of 476 amino acid residues and there existed ten putative transmembrane domains. Figure 46 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein.

25 The search of the protein database using the amino

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acid sequence of the present protein revealed that the protein was similar to Caenorhabditis elegans tetracycline resistance protein-like protein (Accession No. CAA94337). Table 27 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and C. elegans tetracycline resistance protein-like protein (CP). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 51.5% in the intermediate region of 196 amino acid residues.

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Table 27	
${\tt HP\ MAGSDTAPFLSQADDPDDGPVPGTPGLPGSTGNPKSEEPEVPDQEGLQRITGLSPGRSADDPDDGPVPGTPGLSPGRSADDPDDGPVPGTPGTPGTPGTPGTPGTPGTPGTPGTPGTPGTPGTPGTP$	L
CP MVNSQQDY	· II
HP IVAVLCYINLLNYMDRFTVAGVLPDIEQFFNIGDSSSGLIQTVFISSYMVLAPVFGYLG	Đ
**  . *****. **. ****** **. ** . ******	‡
CP SYTALFYVNLLNYYDRYTVAGYLTQYQTYYNISDSLGGLIQTYFLISFMYFSPYCGYLG	D
HP RYNRKYLMCGGIAFWSLVTLGSSFIPGEHFWLLLLTRGLVGVGEASYSTIAPTLIADLF	Y
*. *** *   * *   *****. * **. * **. **	
CP RFNRKWIMIIGVGIWLGAVLGSSFVPANHFWLFLVLRSFVGIGEASYSNVAPSLISDMF	N
HP ADQRSRMLSIFYFAIPVGSGLGYIAGSKVKDMAGDWHWALRYTPGLGVVAVLLLFLVVR	_
** **************** * * * * *	*
CP GQKRSTVFMIFYFAIPVGSGLGFIVGSNVATLTGHWQWGIRVSAIAGLIVMIALVLFTY	E
HP PPRGAVERHSDLPPLNPTSWWADLRALARNLIFGLITCLTGVLGVGLGVEISRRLRHSNI * ***	P
CP PERGAADKAMGESKDVVVTTNTTYLEDLVILLKTPTLVACTWGYTALVFVSGTLSWWEPT	Γ
HP RADPLVCATGLLGSAPFLFLSLACARGSIVATYIFIFIGETLLSMNWAIVADILLYVVII	•
CP VIQHLTAWHQGLNDTKDLASTDKDRVALYFGAITTAGGLIGVIFGSMLSKWLVAGWGPFR	2
HP TRRSTAEAFQIVLSHLLGDAGSPYLIGLISDRLRRNWPPSFLSEFRALQFSLMLCAFVGA	1
CP RLOTDRAOPLVAGGGALLAAPFLLIGMIFGDKSLVLLYIMIFRGITTDMGDAWGLALDUUT	

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## HP LGGAAFLGTAIFIEADRRRAQLHVQGLLHEAGSTDDRIVVPQRGRSTRVPVASVLI CP TVIHPNRRSTAFSYFVLVSHLFGDASGPYLIGLISDAIRHGSTYPKDQYHSLVSATYCCV

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA460778) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention. Furthermore, the search has revealed the registration of sequences that shared a homology of 90% or more (Accession No. E12646) in patent data. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10750> (SEQ ID NOS: 127, 137, and 147)

Determination of the whole base sequence of the cDNA insert of clone HP10750 obtained from cDNA library of human umbilical cord blood revealed the structure consisting of a 262-bp 5'-untranslated region, a 1350-bp ORF, and a 564-bp 3'-untranslated region. The ORF encodes a protein consisting of 449 amino acid residues and there existed four putative transmembrane domains. Figure 47 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-

Doolittle method, of the present protein.

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The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AW304031) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

<HP10777> (SEQ ID NOS: 128, 138, and 148)

Determination of the whole base sequence of the cDNA insert of clone HP10777 obtained from cDNA library of human kidney revealed the structure consisting of a 15-bp 5'-untranslated region, a 318-bp ORF, and a 1030-bp 3'untranslated region. The ORF encodes a protein consisting of 105 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 48 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 14 kDa that was somewhat larger than the molecular weight of 11,603 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 30.

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Determination of the whole base sequence of the cDNA insert of clone HP10780 obtained from cDNA library of human kidney revealed the structure consisting of a 226-bp 5'-untranslated region, a 246-bp ORF, and a 571-bp 3'untranslated region. The ORF encodes a protein consisting of 81 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 49 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. translation resulted in formation of a translation product of 10 kDa that was somewhat larger than the molecular weight of 8,533 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 6 kDa. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 25.

The search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA658245) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

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Determination of the whole base sequence of the cDNA insert of clone HP10795 obtained from cDNA library of human kidney revealed the structure consisting of a 356-bp 5'-untranslated region, a 1659-bp ORF, and a 420-bp 3'untranslated region. The ORF encodes a protein consisting of 552 amino acid residues and there existed one transmembrane N-terminus. Figure 50 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. translation resulted in formation of a translation product of 65 kDa that was almost identical with the molecular weight of 64,280 predicted from the ORF.

The search of the protein database using the amino acid sequence of the present protein revealed that the protein was similar to human UDP-N-acetyl- $\alpha$ -Dgalactosamine:polypeptide N-acetylgalactosaminyltransferase 2 (Accession No. NP 004472). Table 28 shows the comparison between amino acid sequences of the human protein of the human UDP-N-acetyl-α-D-(HP) and invention galactosamine:polypeptide N-acetylgalactosaminyltransferase 2 (GA). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 49.9% in the entire

region other than the N-terminal region.

Tabl	e 28
HP	MRRLTRRLVLPVFGVLWITVLLFFWVTKRKLEVPT
GA	MRRRSRMLLCFAFLWYLGIAYYMYSGGGSALAGGAGGGAGRKEDWNEIDPIKKKDLHHSN
HP	GPEVQTPKPSDADWDDLWDQFDERRYLNAKKWRVGDDPYKLYAFNQRESERISSNRAIPD
	* * * . * * * . *
GA	GEEKAQSMETLPPGKVRWPDFNQEAYVGGTMVRSGQDPYARNKFNQVESDKLRMDRAIPI
ĦР	TRHLRCTLLVYCTDLPPTSIIITFHNEARSTLLRTIRSVLNRTPTHLIREIILVDDFSNI
	*** . * ***. ** ******** ****. *** *. *
GA	TRHDQCQRKQWRYDLPATSVVITFHNEARSALLRTVVSVLKKSPPHLIKEIILVDDYSNI
HP	PDDCKQLIKLPKVKCLRNNERQGLVRSRIRGADIAQGTTLTFLDSHCEVNRDWLQPLLHI
	*. * * * . **. ***. * ** *** *** ** . * * * . * * . * * . * * . * * . *
GA	PEDGALLGKIEKVRVLRNDRREGLMRSRVRGADAAQAKVLTFLDSHCECNEHWLEPLLEI
HP	VKEDYTRVVCPVIDIINLDTFTYIESASELRGGFDWSLHFQWEQLSPEQ-KARRLDPTE
	* ** ****, *, **, **, *, * *, *, *****, * *, *, *** *, . *,
GA	VAEDRTRVVSPIIDVINMDNFQYVGASADLKGGFDWNLVFKWDYMTPEQRRSRQGNPVA
HI	PIRTPIIAGGLFVIDKAWFDYLGKYDMDMDIWGGENFEISFRVWMCGGSLEIVPCSRVGH
	*. **. ****** ** . *. ****** **. ****** ******
G	A IKTPMIAGGLEVMDKEYFEELGKYDMMMDVWGGENLEISERVWQCGGSLEIIPCSRVGH

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HP ASHLCLDTDMFGDGTENGKEIVVNPCESSLMSQHWDMVSS

GA GSNLCLDS---R-TAKSGGLSYEVCGPAL-SQQWKFTLNLQQ

of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA160076) among ESTs. However, since they are partial sequences, it can not be judged whether or not they encode the same protein as the protein of the present invention.

## INDUSTRIAL APPLICABILITY

The present invention provides human proteins having hydrophobic domains, DNAs encoding these proteins,

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expression vectors for these DNAs and eukaryotic cells expressing these DNAs. Since all of the proteins of the present invention are secreted or exist in the cell membrane, they are considered to be proteins controlling the proliferation and/or the differentiation of the cells. Accordingly, the proteins of the present invention can be employed as pharmaceuticals such as carcinostatic agents which act to control the proliferation and/or differentiation of the cells, or as antigens for preparing antibodies against these proteins. The DNAs of the present invention can be utilized as probes for the genetic diagnosis and gene sources for the gene therapy. Furthermore, the DNAs can be utilized for expressing these proteins in large quantities. Cells into which these genes are introduced to express these proteins can be utilized for detection of the corresponding receptors or ligands, screening of novel small molecule pharmaceuticals and the like. The antibody of the present invention can be utilized for the detection, quantification, purification and the like of the protein of the present invention.

The present invention also provides genes corresponding to the polynucleotide sequences disclosed herein. "Corresponding genes" are the regions of the genome that are transcribed to produce the mRNAs from which cDNA polynucleotide sequences are derived and may include

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contiguous regions of the genome necessary for the regulated expression of such genes. Corresponding genes may therefore include but are not limited to coding sequences, 5' and 3' untranslated regions, alternatively spliced exons, introns, promoters, enhancers, and silencer or suppressor elements. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or disclosed sequence from the information identification and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. An "isolated gene" is a gene that has been separated from the adjacent coding sequences, if any, present in the genome of the organism from which the gene was isolated.

Organisms that have enhanced, reduced, or modified expression of the gene(s) corresponding to the polynucleotide sequences disclosed herein are provided. The desired change in gene expression can be achieved through the use of antisense polynucleotides or ribozymes that bind and/or cleave the mRNA transcribed from the gene (Albert and Morris, 1994, Trends Pharmacol. Sci. 15(7): 250-254; Lavarosky et al., 1997, Biochem. Mol. Med. 62(1): 11-22; and Hampel, 1998, Prog. Nucleic Acid Res. Mol. Biol. 58: 1-39; all of which are incorporated by reference herein). Transgenic animals that have multiple copies of the gene(s)

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corresponding to the polynucleotide sequences disclosed herein, preferably produced by transformation of cells with genetic constructs that are stably maintained within the transformed cells and their progeny, are provided. Transgenic animals that have modified genetic control regions that increase or reduce gene expression levels, or that change temporal or spatial patterns of gene expression, are also provided (see European Patent No. 0 649 464 B1, incorporated by reference herein). In addition, organisms are provided in which the gene(s) corresponding to the polynucleotide sequences disclosed herein have partially or completely inactivated, through insertion of extraneous sequences into the corresponding gene(s) or through deletion of all or part of the corresponding gene(s). Partial or complete gene inactivation can be accomplished through insertion, preferably followed by imprecise excision, of transposable elements (Plasterk, 1992, Bioessays 14(9): 629-633; Zwaal et al., 1993, Proc. Natl. Acad. Sci. USA 90(16): 7431-7435; Clark et al., 1994, Proc. Natl. Acad. Sci. USA 91(2): 719-722; all of which are incorporated by reference herein), or through homologous recombination, preferably detected by positive/negative genetic selection strategies (Mansour et al., 1988, Nature 336: 348-352; U.S. Patent Nos. 5,464,764; 5,487,992; 5,627,059; 5,631,153; 5,614, 396; 5,616,491; and 5,679,523; all of which are

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incorporated by reference herein). These organisms with altered gene expression are preferably eukaryotes and more preferably are mammals. Such organisms are useful for the development of non-human models for the study of disorders involving the corresponding gene(s), and for the development of assay systems for the identification of molecules that interact with the protein product(s) of the corresponding gene(s).

Where the protein of the present invention is membrane-bound (e.g., is a receptor), the present invention also provides for soluble forms of such protein. In such forms part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and transmembrane domains of proteins of the invention can be identified in accordance with known techniques for determination of such domains from sequence information.

Proteins and protein fragments of the present invention include proteins with amino acid sequence lengths that are at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of a disclosed protein and have at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with that disclosed protein, where

sequence identity is determined by comparing the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Also included in the present invention are proteins and protein fragments that contain a segment preferably comprising 8 or more (more preferably 20 or more, most preferably 30 or more) contiguous amino acids that shares at least 75% sequence identity (more preferably, at least 85% identity; most preferably at least 95% identity) with any such segment of any of the disclosed proteins.

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Species homologs of the disclosed polynucleotides and proteins are also provided by the present invention. As used herein, a "species homologue" is a protein or polynucleotide with a different species of origin from that of a given protein or polynucleotide, but with significant sequence similarity to the given protein or polynucleotide, as determined by those of skill in the art. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally-occurring alternative forms of the isolated polynucleotide which also encode proteins which are identical, homologous, or related to that encoded by the

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polynucleotides.

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The invention also includes polynucleotides with sequences complementary to those of the polynucleotides disclosed herein.

The present invention also includes polynucleotides capable of hybridizing under reduced stringency conditions, more preferably stringent conditions, and most preferably highly stringent conditions, to polynucleotides described herein. Examples of stringency conditions are shown in the table below: highly stringent conditions are those that are at least as stringent as, for example, conditions A-F; stringent conditions are at least as stringent as, for example, conditions are at least as stringent as, for example, conditions G-L; and reduced stringency conditions are at least as stringent as, for example, conditions M-R.

Table 29

Stringency	Poly-	Hybrid	Hybridization Temperature	Wash
Condition	nucleotide	Length	and Buffer	Temperature
	Hybrid ·	(bp) *	·	and Buffer
A	DNA: DNA	≥50	65°C; 1×SSC -or-	65°C; ·
	Divis Divis		42°C; 1×SSC,50%	0.3×SSC
			formamide	
В	DNA: DNA	<50	T <sub>B</sub> *; 1×SSC	T <sub>B</sub> *; 1×SSC
С	DNA: RNA	≥50	67°C; 1×SSC -or-	67°C;
	DIM : NAM		45°C; 1×SSC,50%	0.3×SSC
			formamide	
D	DNA: RNA	<50	Tp*; 1×SSC	Tp*; 1×SSC
Е	RNA: RNA	≥50	70°C; 1×SSC -or-	70°C;
-	KNA . KNA	230	50°C; 1×SSC,50%	0.3×SSC
	:		formamide	0.57550
F	DAYN . DAYN	<50	T <sub>r</sub> *; 1×SSC	T <sub>F</sub> *; 1×SSC
	RNA: RNA			
G	DNA: DNA	≥50	65°C; 4×SSC -or-	65°C; 1×SSC
			42°C; 4×SSC,50%	
			formamide	
Н	DNA: DNA	<50	T <sub>H</sub> *; 4×SSC	T <sub>H</sub> *; 4×SSC
I	DNA: RNA	≥50	67°C; 4×SSC -or-	67°C; 1×SSC
			45°C; 4×SSC,50%	
			formamide	
J	DNA: RNA	<50	T <sub>J</sub> *; 4×SSC	T <sub>J</sub> *; 4×SSC
K	RNA: RNA	≥50	70°C; 4×SSC -or-	67°C; 1×SSC
			50°C; 4×SSC,50%	İ
			formamide	
L	RNA: RNA	<50	T <sub>L</sub> *; 2×SSC	T <sub>L</sub> *; 2×SSC
M	DNA: DNA	≥50	50°C; 4×SSC -or-	50°C; 2×SSC
	1		40°C; 6×SSC,50%	
			formamide	
N	DNA: DNA	<50	T <sub>N</sub> *; 6×SSC	T <sub>N</sub> *; 6×SSC
0	DNA: RNA	≥50	55°C; 4×SSC -or-	55°C; 2×SSC
			42°C; 6×SSC,50%	
			formamide	
P	DNA: RNA	<50	T <sub>p</sub> *; 6×SSC	Tp*; 6×SSC
Q	RNA: RNA	≥50	60°C; 4×SSC -or-	60°C; 2×SSC
_			45°C; 6×SSC,50%	·
			formamide	•
R	RNA: RNA	<50	T <sub>R</sub> *; 4×SSC	T <sub>R</sub> *; 4×SSC
				•

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- ‡: The hybrid length is that anticipated for the hybridized region(s) of the hybridizing polynucleotides. When hybridizing a polynucleotide to a target polynucleotide of unknown sequence, the hybrid length is assumed to be that of the hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence complementarity.
- t: SSPE (1×SSPE is 0.15M NaCl, 10mM NaH<sub>2</sub>PO<sub>4</sub>, and 1.25mM EDTA, pH7.4) can be substituted for SSC (1×SSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after hybridization is complete.
- \*T<sub>B</sub> T<sub>R</sub>: The hybridization temperature for hybrids
  anticipated to be less than 50 base pairs in length should
  be 5-10°C less than the melting temperature (T<sub>m</sub>) of the
  hybrid, where T<sub>m</sub> is determined according to the following
  equations. For hybrids less than 18 base pairs in length,

  T<sub>m</sub>(°C)=2(#of A + T bases) + 4(# of G + C bases). For hybrids
  between 18 and 49 base pairs in length, T<sub>m</sub>(°C)=81.5 +
  16.6(log<sub>10</sub>[Na<sup>+</sup>]) + 0.41 (%G+C) (600/N), where N is the
  number of bases in the hybrid, and [Na<sup>+</sup>] is the concentration
  of sodium ions in the hybridization buffer ([Na<sup>+</sup>] for
  1×SSC=0.165M).

Additional examples of stringency conditions for polynucleotide hybridization are provided in Sambrook, J., E.F. Fritsch, and T. Maniatis, 1989, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and Current Protocols in Molecular Biology, 1995, F.M. Ausubel et al., eds., John Wiley & Sons, Inc., sections 2.10 and 6.3-6.4, incorporated herein by reference.

Preferably, each such hybridizing polynucleotide has a length that is at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of the polynucleotide of the present invention to which it hybridizes, and has at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with the polynucleotide of the present invention to which it hybridizes, where sequence identity is determined by comparing the sequences of the hybridizing polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps.

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## CLAIMS

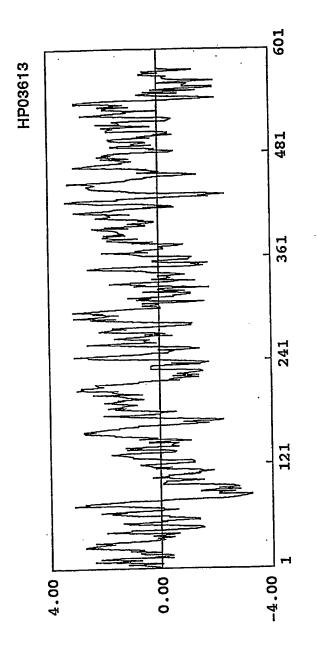
1. A protein comprising any one of amino acid sequences selected from the group consisting of SEQ ID NOS: 1 to 10, 31 to 40, 61 to 70, 91 to 100 and 121 to 130.

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- 2. An isolated DNA encoding the protein according to Claim 1.
- 3. An isolated cDNA comprising any one of base sequences selected from the group consisting of SEQ ID NOS: 11 to 20, 41 to 50, 71 to 80, 101 to 110 and 131 to 140.
  - 4. The cDNA according to Claim 3 consisting of any one of base sequences selected from the group consisting of SEQ ID NOS: 21 to 30, 51 to 60, 81 to 90, 111 to 120 and 141 to 150.
- 5. An expression vector that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 by in vitro translation or in eukaryotic cells.
  - 6. A transformed eukaryotic cell that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 and of producing the protein according to Claim 1.
  - 7. An antibody directed to the protein according to Claim 1.



Amino Acid Residue Number

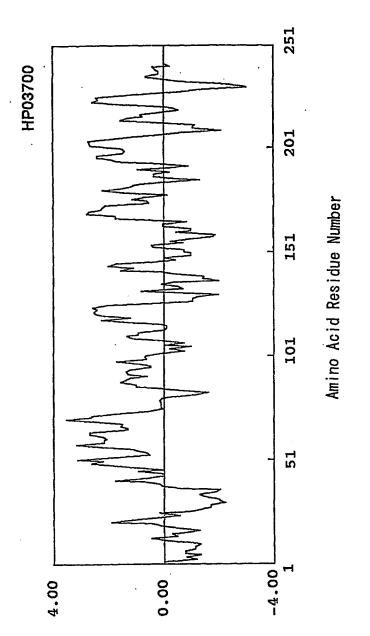
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Hydrophilicity/Hydrophobicity

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(d)

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Hydrophilicity/Hydrophobicity

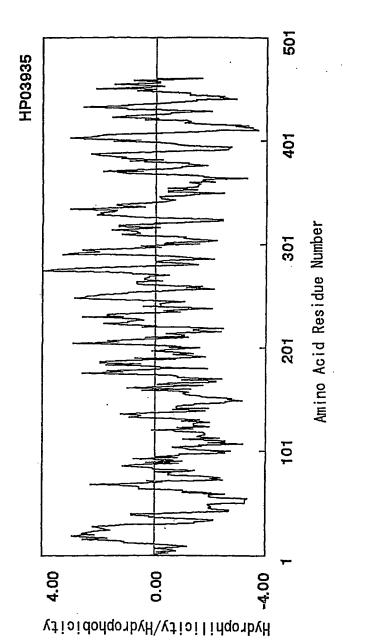
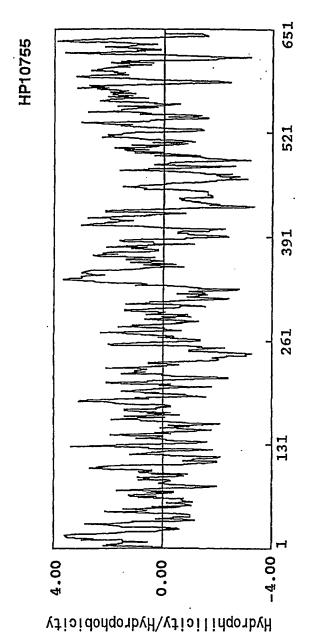


Fig. 3



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Amino Acid Residue Number

Fig. 4

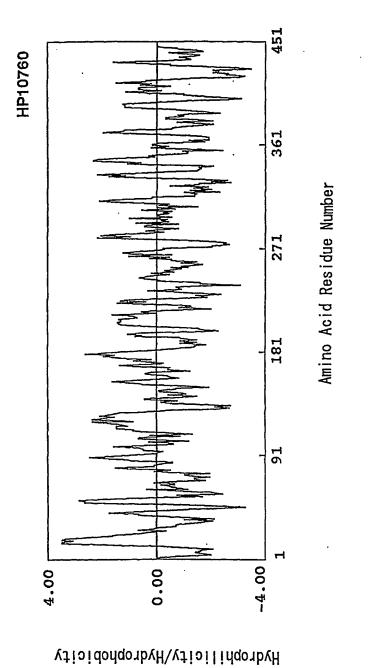
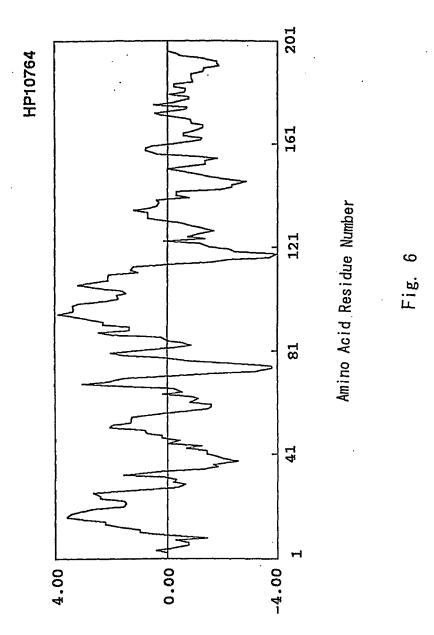
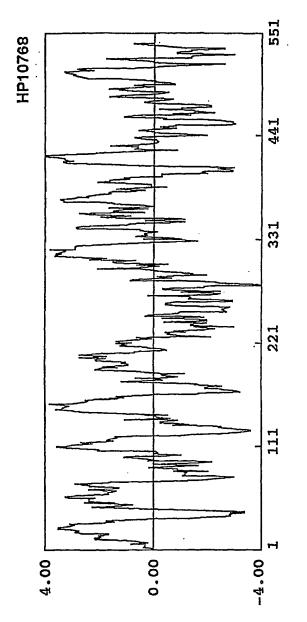


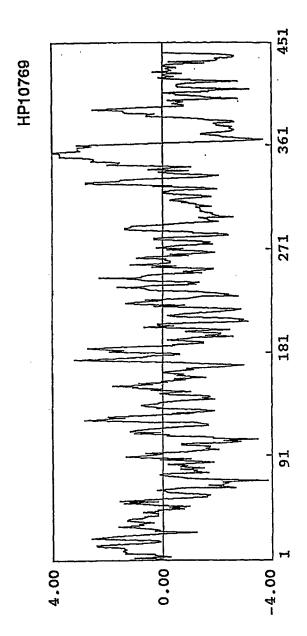
Fig. 5



Hydrophilicity/Hydrophobicity

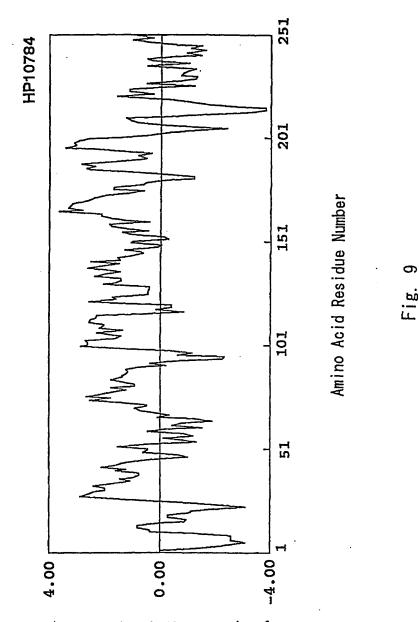


Hydrophilicity/Hydrophobicity

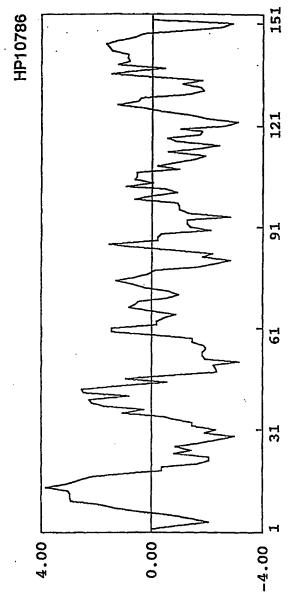


Hydrophilicity/Hydrophobicity

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Hydrophilicity/Hydrophobicity

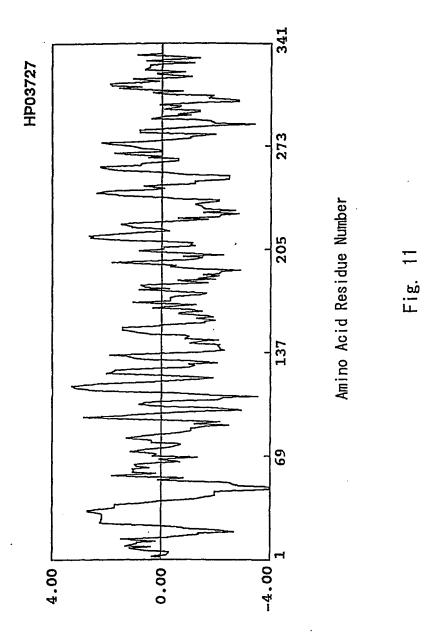


Hydrophilicity/Hydrophobicity

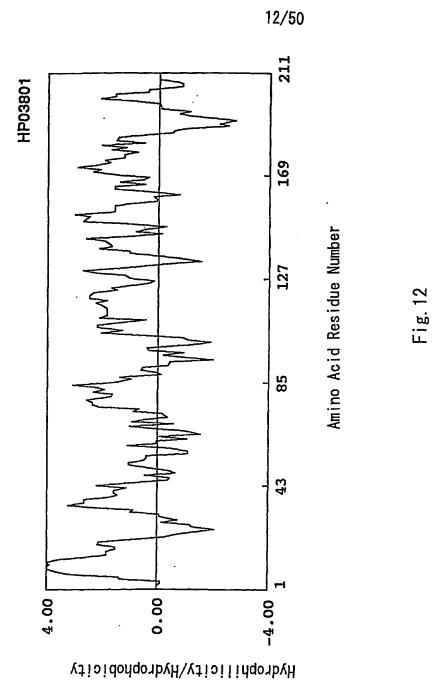
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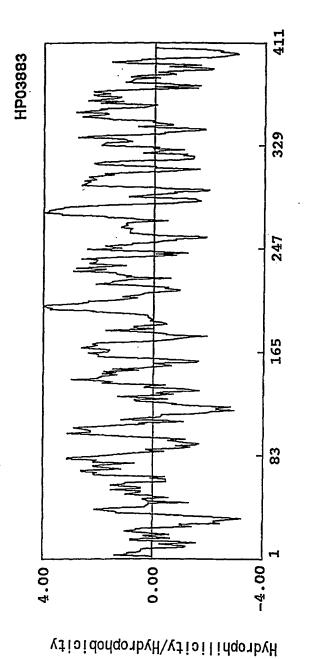
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Fig.



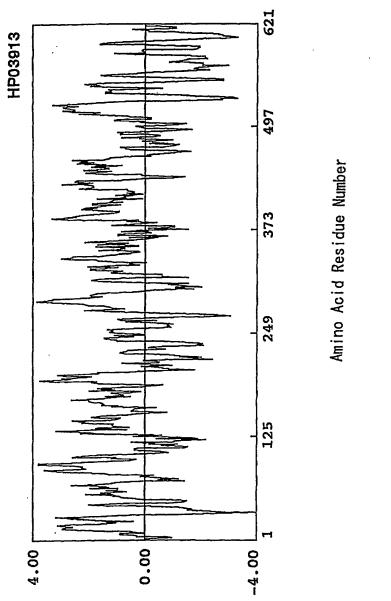
Hydrophilicity/Hydrophobicity



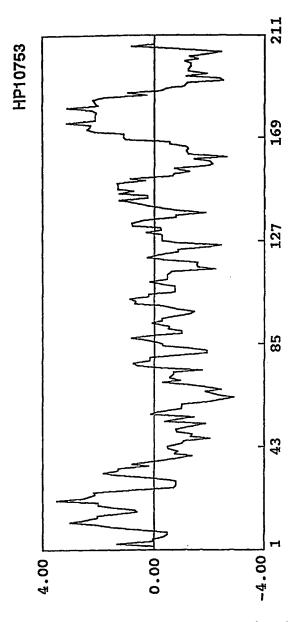


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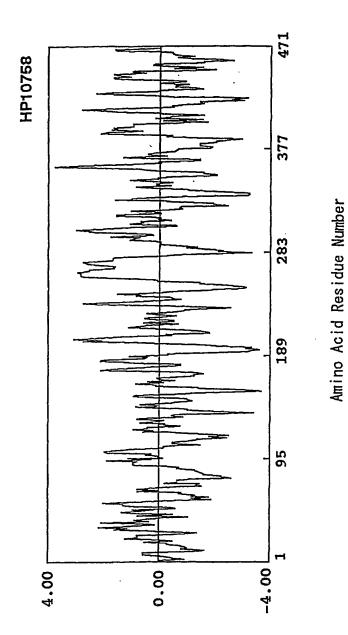


Hydrophilicity/Hydrophobicity



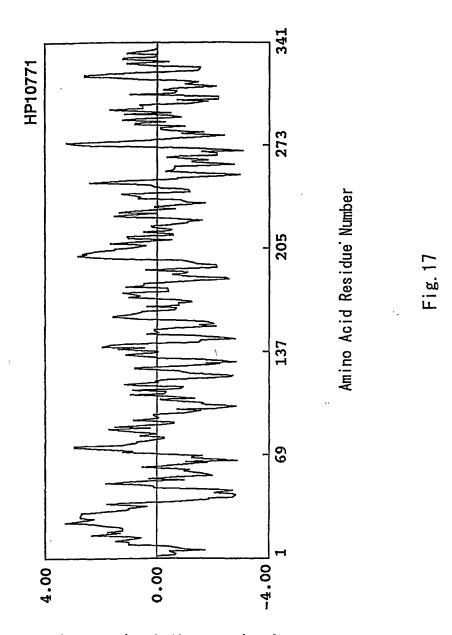
Hydrophilicity/Hydrophobicity

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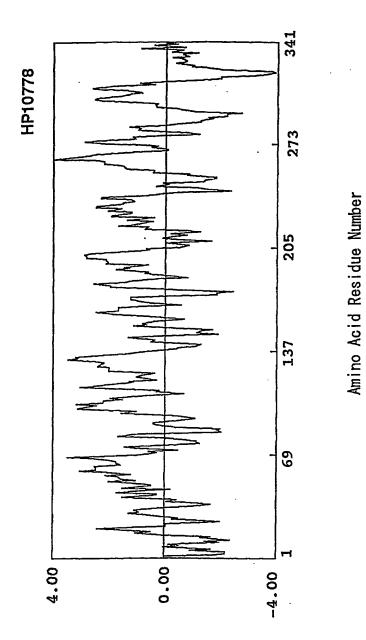


Hydrophilicity/Hydrophobicity

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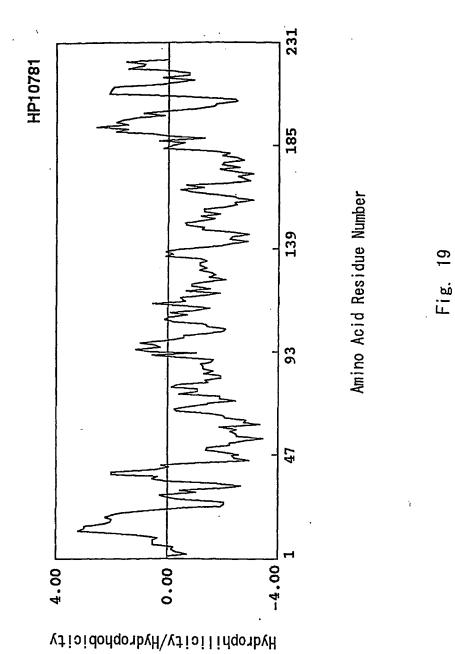


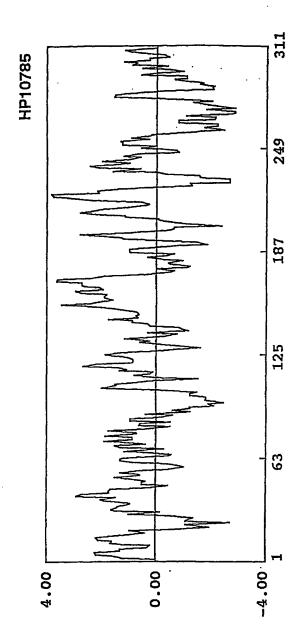
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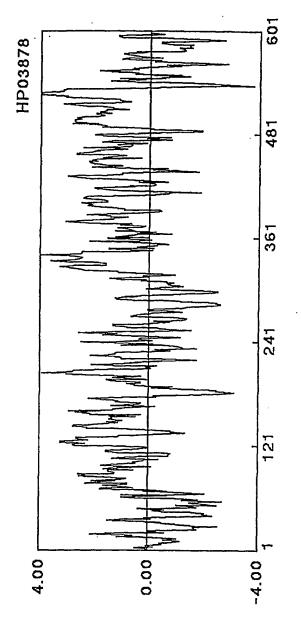
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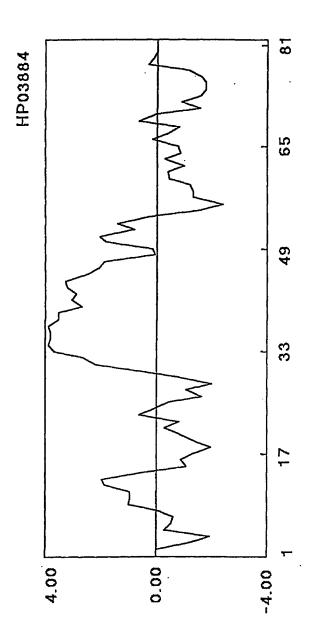


 $\hbox{\it H} \lambda \hbox{\it q} \hbox{\it kobbilicity} \\$ 



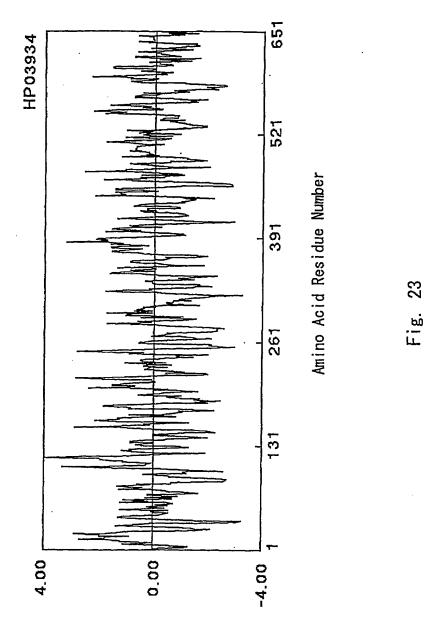
Hydrophilicity/Hydrophobicity



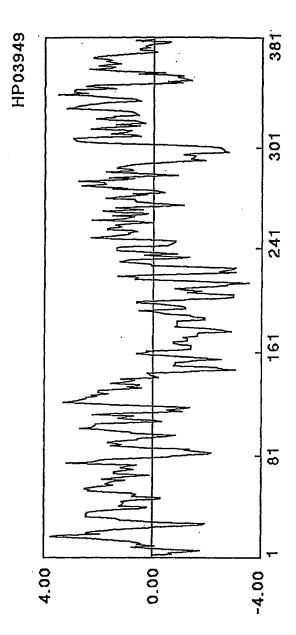


Hydrophilicity/Hydrophobicity

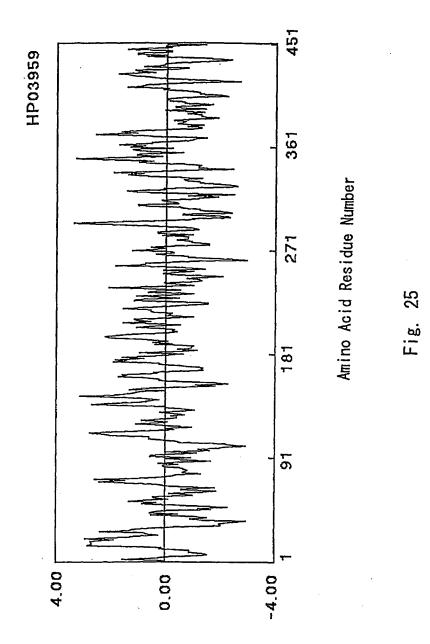
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Hydrophilicity/Hydrophobicity



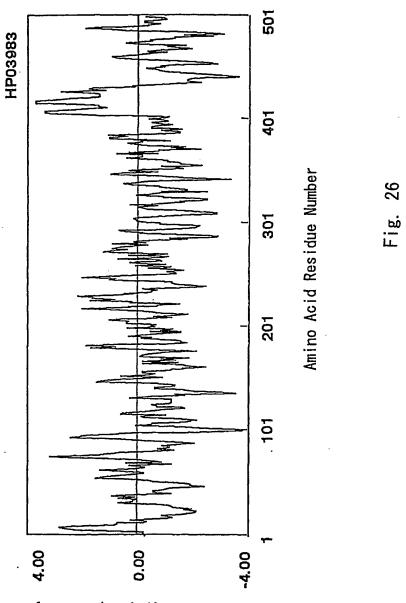
Amino Acid Residue Number



Hydrophilicity/Hydrophobicity

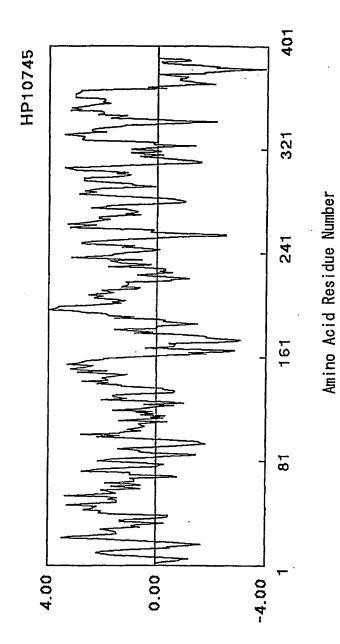
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26/50

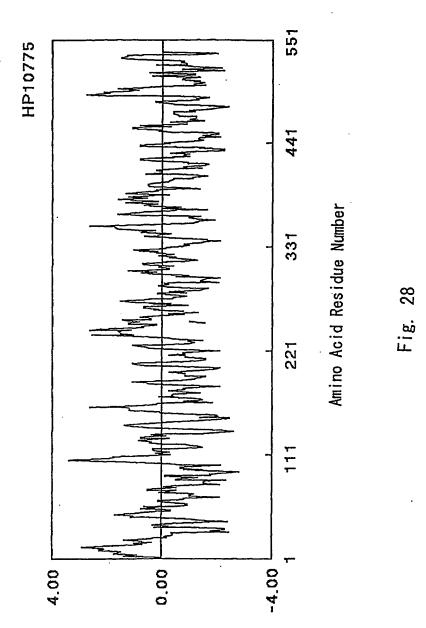


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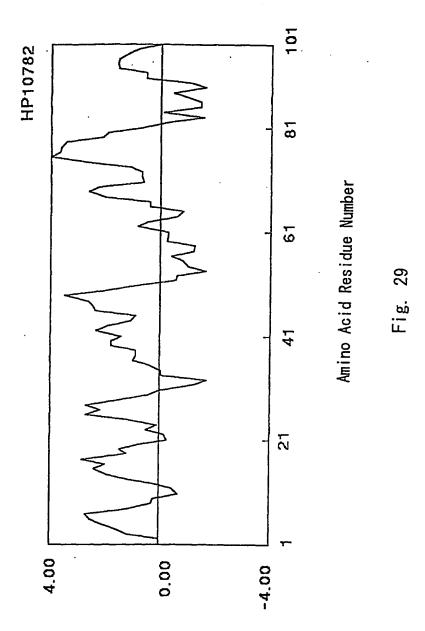




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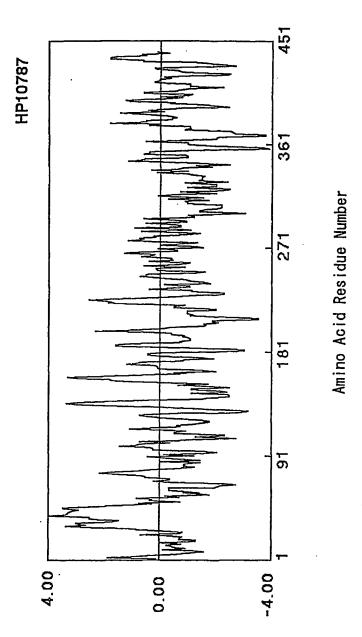


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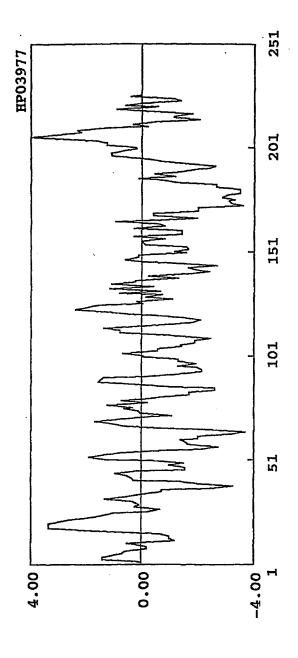


Hydrophilicity/Hydrophobicity

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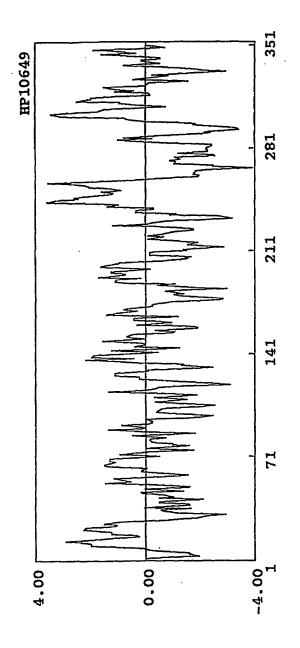


 ${\tt H} \lambda {\tt qtobbillicify/H} \lambda {\tt qtobbobicify}$ 

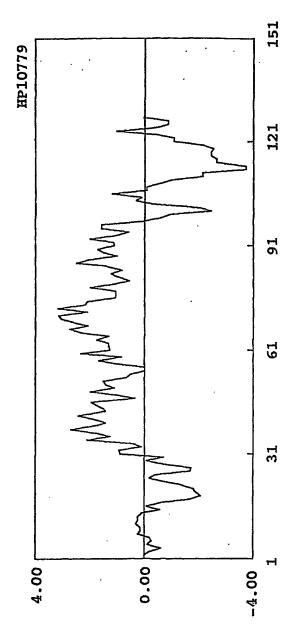


 $H\lambda drophilicity/Hy drophobicity$ 

Amino Acid Residue Number



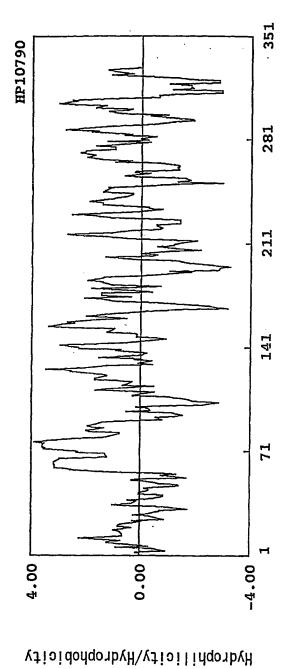
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Hydrophilicity/Hydrophobicity

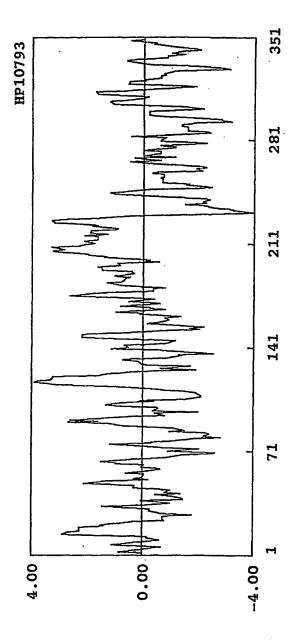
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·ig. 33



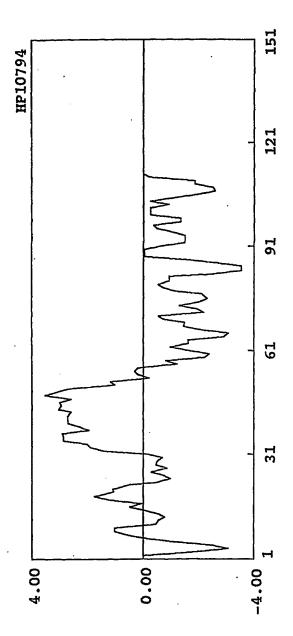
Amino Acid Residue Number

ig. 34



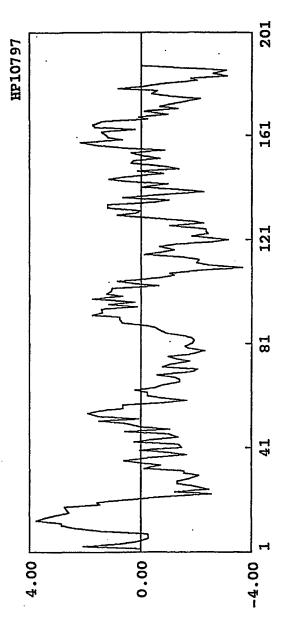
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Amino Acid Residue Number

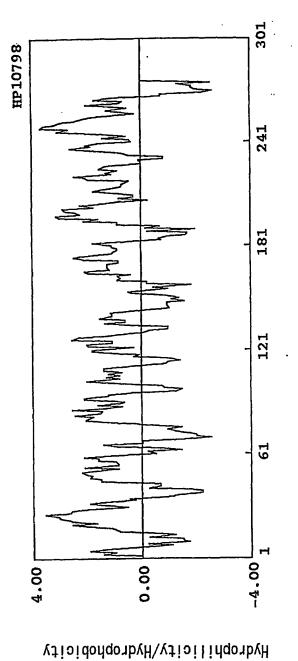


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Amino Acid Residue Number

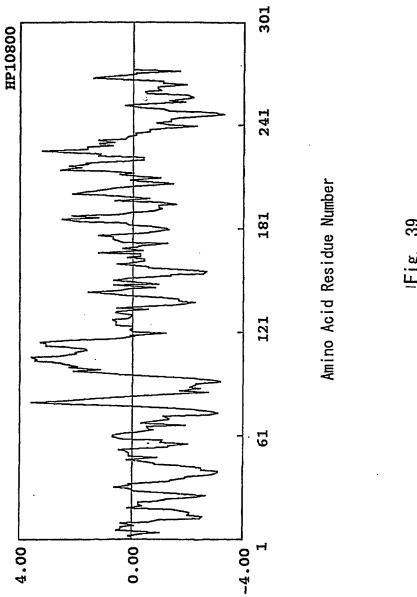


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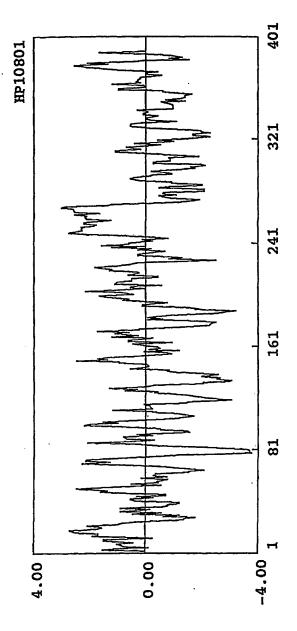
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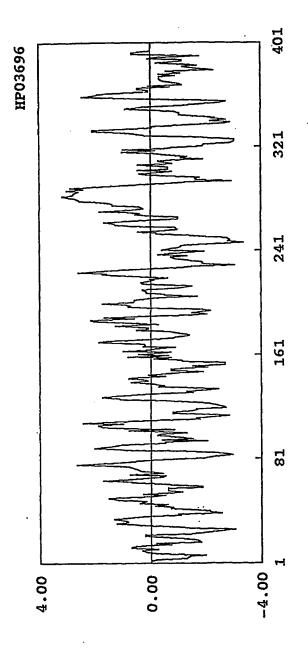
Hydrophilicity/Hydrophobicity

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Hydrophilicity/Hydrophobicity

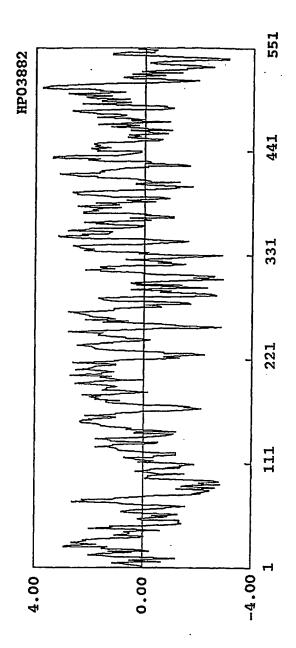
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Hydrophilicity/Hydrophobicity

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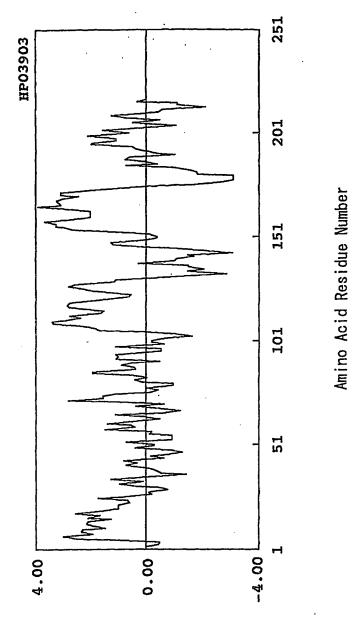
Fig A1



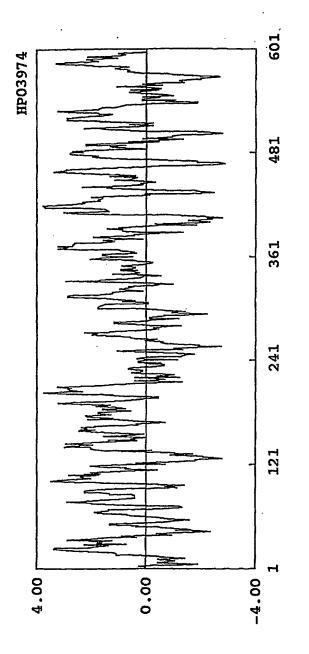
Hydrophilicity/Hydrophobicity

Fig 42

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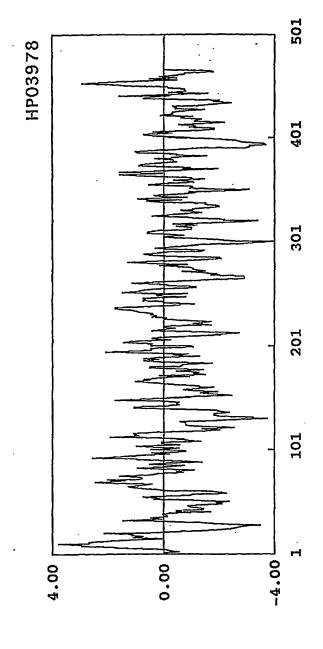
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Amino Acid Residue Number

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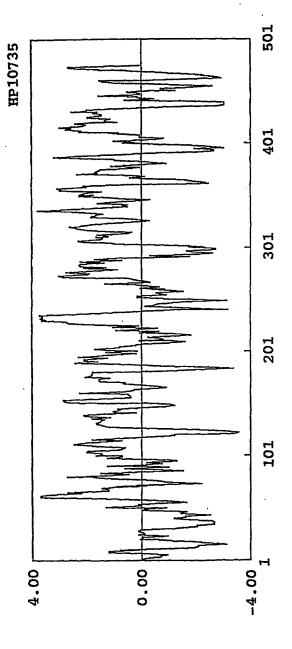
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Hydrophilicity/Hydrophobicity

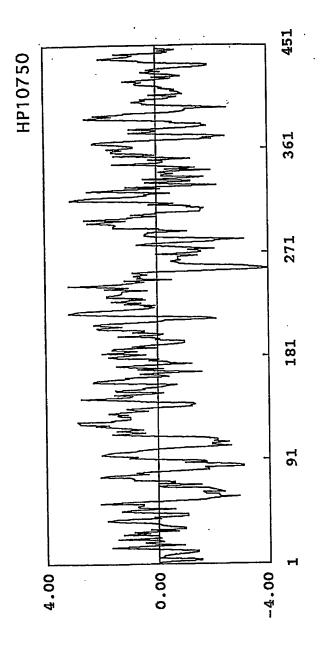
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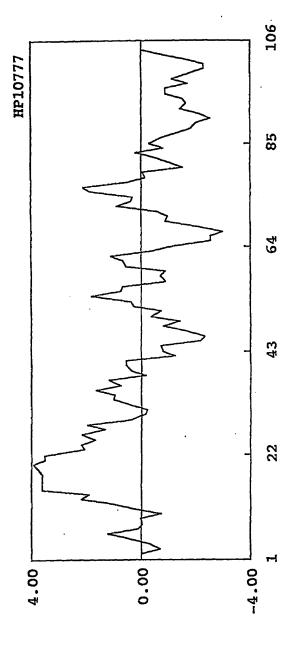


Amino Acid Residue Number Fig. 46

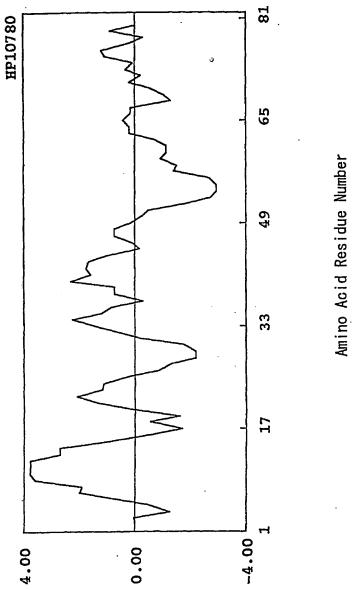
 ${\tt H} \lambda {\tt q} \kappa {\tt ob} {\tt hilicity} {\tt H} \lambda {\tt q} \kappa {\tt ob} {\tt hob} {\tt icity}$ 

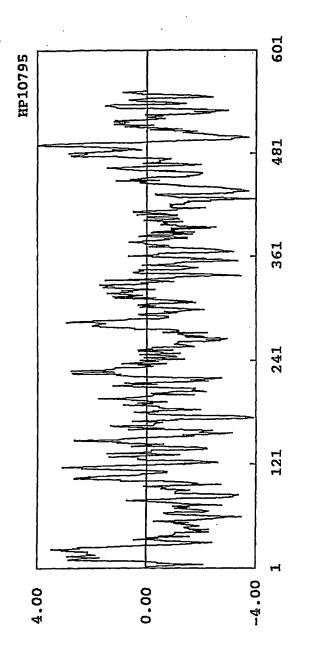


Amino Acid Residue Number



Amino Acid Residue Number





 $H\lambda drophilicity/Hy drophobicity$ 

Amino Acid Residue Number

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Sagami Chemical Research Center

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Gly Ser Leu Ser Pro Glu Ala Leu Leu Ala Ile Ser Ile Pro Pro Gly

65 70 75 80

Pro Asn Gln Arg Pro His Gln Cys Arg Arg Phe Arg Gln Pro Gln Trp

85 90 95

20 Gln Leu Leu Asp Pro Asn Ala Thr Ala Thr Ser Trp Ser Glu Ala Asp

100 105 110

Thr Glu Pro Cys Val Asp Gly Trp Val Tyr Asp Arg Ser Ile Phe Thr

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Ser Thr Ile Val Ala Lys Trp Asn Leu Val Cys Asp Ser His Ala Leu

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10	Phe	Arġ	Glu	Glu	Glu	Cys	Ser	Cys	Val	Cys	Asp	Ile	Gly	Tyr	Gly	Gly
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	Ala	Gln	Cys	Ala	Thr	Lys	Val	His	Phe	Pro	Phe	His	Thr	Cys	Asp	Leu
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	Tyr	Arg	Ala	Arg	Met	Lys	Cys	Gln	Arg	Lys	Gly	Gly	Val	Leu	Ala	Gln
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	65					70					75					80
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	Val Ar	j Lys	Tyr	Gln	Ser	Arg	Arg	Glu	Ser	Glu	Val	Val		Thr	Ile
25		35					40					45			

	Thr	Ala	Ile	Phe	Ser	Leu	Ala	Ile	Ala	Leu	Ile	Thr	Ser	Ala	Leu	Leu
		50			v		55					60				
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				100					105					110		
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	385					390					395					400
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	Ala	Ala	Gly	Gly	Val	Leu	Gly	Gly	Trp	Leu	Val	Asp	Arg	Ala	Gly	Arg
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#### 27 /346

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#### 31 /346

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34 /346

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40 /346

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#### 43 /346

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### 44 /346

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	Leu Asp A	Ala Glu V	al Leu Gl	u Val Phe	His Pro Th	nr His Glu T	rp Gln
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	Ala Leu (	Gln Pro G	ly Gln Al	la Val Pro	Ala Gly Se	er His Val <i>F</i>	arg Leu
		80		85		90	
	aat ctt	cag act o	ggg gaa a	ga gag gca	aaa ctc c	aa tat gag q	gac aag 399
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	Asp	Phe	Ser	Leu	Arg	Ile	Glu	Pro	Leu	Glu	Val	Ala	Asp	Glu	Gly	Thr	
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	Tyr	Ser	Cys	His	Leu	His	His	His	Tyr	Cys	Gly	Leu	His	Glu	Arg	Arg	
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	Gly	Ser	Pro	Gly	Asn	Gly	Ser	Ser	His	Ser	Gly	Ala	Pro	Gly	Pro	Asp	
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	ccc	aca	ctg	gcg	cgc	ggc	cac	aac	gtc	atc	aat	gtc	atc	gtc	ccc	gag	1010
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	Ser	Arg	Ala	His	Phe	Phe	Gln	Gln	Leu	Gly	Tyr	Val	Leu	Ala	Thr	Leu	
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	Leu Lys Glu Arg A	la Glu Leu A	la His Ser Pro L	eu Pro Ala Lys Tyr	
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	tgttgctttg ggccac	tgg ggctgca	ccc cctgcccttt c	tetgececa tecetacee	t 2007
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20	ccctcccttg gactct	cct gggctgg	agt ctagggetgg g	gctacattt ggcttctgt	a 2127
	ctggctgagg acaggg	agg gagtgaa	gtt ggtttggggt g	gcctgtgtt gccactctc	a 2187
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	ttttt				2252

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	Lys	Leu	Ser	Leu	Leu	Leu	Cys	Ser	Val	Pro	Phe	Val	Ala	Gly	Phe	Ala	
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	Val	Ile	Thr	Ala	Ala	Gln	Asp	Val	Trp	Met	Leu	Leu	Gly	Gly	Arg	Leu	
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	Ser	Leu	Met	Leu	Leu	Leu	Met	Cys	Phe	Met	Pro	Glu	Thr	Pro	Arg	Phe	
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	Cys Gly His Gly Val Gln His Glu Cys Leu Arg Arg Leu Leu Gln Ala	
	225 230 235 240	
	gac cca ggg tgg ccc tgg caa ctc ctc gca cgt ggc cat ctc ggc gcc	828
5	Asp Pro Gly Trp Pro Trp Gln Leu Leu Ala Arg Gly His Leu Gly Ala	
	245 250 255	
	tgt ctc tgc aca gcc tgt tgatgccagc gtggggctgg cctggctggc	876
	Cys Leu Cys Thr Ala Cys	
	260	
10	cgtgggcagc atgtgcctct tcatcgccgg aggtcctcag gccctatgga gccttctggc	936
	ttgcctccgc tttctgcatc ttcagtgtcc ttttcacttt gttctgtgtc cctgaaacta	996
	aaggaaagac tctggaacaa atcacagccc attttgaggg gcgatgacag ccactcacta	1056
	ggggatggag caagcctgtg actccaagct gggcccaagc ccagagcccc tgcctgcccc	1116
	aggggagcca gaatccagcc ccttggagcc ttggtctgca gggtccctcc ttcctgtcat	1176
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	tgctgctctg aggactcagg aacaccttcg agctttgcag acctgcggtc agccctccat	1296
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	aggtgctttt ggaggttggg tgctgggcat tcagtcgctc ctctcacgcg gctgccttat	1416
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	Leu	I.eu	Leu	Val	Leu	Gly	Ala	Ala	Gly	Arg	Gly	Arg	Gly	Gly	Ala	Glu	
10				15					20					25			
	ccc	cgg	gag	ccg	gcg	gac	gga	cag	gcg	ctg	ctg	cgg	ctg	gtg	gtg	gaa	207
	Pro	Arg	Glu	Pro	Ala	Asp	Gly	Gln	Ala	Leu	Leu	Arg	Leu	Val	Val	Glu	
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15	Leu	Val	Gln	Glu	Leu	Arg	Lys	His	His	Ser	Ala	Glu	His	Lys	Gly	Leu	
		45					50					55					
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	Gln	Leu	Leu	Gly	Arg	Asp	Cys	Ala	Leu	Gly	Arg	Ala	Glu	Ala	Ala	Gly	
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	Leu	Gly	Pro	Ser	Pro	Glu	Gln	Arg	Val	Glu	Ile	Val	Pro	Arg	Asp	Leu	
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	agg	atg	aag	gac	aag	ttt	cta	aaa	cac	ctt	aca	ggc	cct	ctt	tat	ttt	399
	Arg	Met	Lys	Asp	Lys	Phe	Leu	Lys	His	Leu	Thr	Gly	Pro	Leu	Tyr	Phe	
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	Ser Pro	Lys Cys	Ser Lys	His Phe	His Arg	Leu Tyr	His Asn	Thr Arg	
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	gac tgc	acc att	cct gca	tac tat	aaa aga	tgc gcc	agg ctt	ctt acc	495
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	cgg ctg	gct gtc	agt cca	gtg tgc	atg gag	gat aag	cag tgag	gcagacc	544
	Arg Leu	Ala Val	Ser Pro	Val Cys	Met Glu	Asp Lys	Gln		
	140		145			150			
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	tgtacttg	ac agtgt	tatct g	tcacttati	taaaaaa	aaa aca	caaaagg a	atgctccac	784
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	tggtcgtt	tg tatta	ataaat gi	aaaatagt	attccago	cta ttg	tgcaata t	gtaaatagt	1084
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<212> PRT

<213> Homo sapiens

25 <400> 31

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5	Val	Ala	Leu	Gly	Thr	Val	Ala	Trp	Arg	Arg	Ala	Trp	Pro	Arg	Arg	Arg
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	Arg	Arg	Leu	Gln	Gln	Val	Gly	Thr	Val	Ala	Lys	Leu	Trp	Ile	Tyr	Pro
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	Val	Lys	Ser	Cys	Lys	Gly	Val	Pro	Val	Ser	Glu	Ala	Glu	Cys	Thr	Ala
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	Met	Gly	Leu	Arg	Ser	Gly	Asn	Leu	Arg	Asp	Arg	Phe	Trp	Leu	Val	Ile
					85					90					95	
	Lys	Glu	Asp	Gly	His	Met	Val	Thr	Ala	Arg	Gln	Glu	Pro	Arg	Leu	Val
				100					105					110		
15	Leu	Ile	Ser	Ile	Ile	Tyr	Glu	Asn	Asn	Cys	Leu	Ile	Phe	Arg	Ala	Pro
			115					120					125			
	Asp	Met	Asp	Gln	Leu	Val	Leu	Pro	Ser	Lys	Gln	Pro	Ser	Ser	Asn	Lys
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	Leu	His	Asn	Cys	Arg	Ile	Phe	Gly	Leu	Asp	Ile	Lys	Gly	Arg	Asp	Суѕ
20	145					150					155					160
	Gly	Asn	Glu	Ala	Ala	Lys	Trp	Phe	Thr	Asn	Phe	Leu	Lys	Thr	Glu	Ala
					165					170	i				175	
	Tyr	Arg	Leu	Val	Gln	Phe	Glu	Thr	Asn	Met	Lys	Gly	Arg	Thr	Ser	Arg
				180	ı				185					190	١	
25	Lys	Leu	Leu	Pro	Thr	Leu	Asp	Gln	Asn	Phe	Gln	Val	Ala	Tyr	Pro	Asp

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Tyr Cys Pro Leu Leu Ile Met Thr Asp Ala Ser Leu Val Asp Leu Asn Thr Arg Met Glu Lys Lys Met Lys Met Glu Asn Phe Arg Pro Asn Ile Val Val Thr Gly Cys Asp Ala Phe Glu Glu Asp Thr Trp Asp Glu Leu Leu Ile Gly Ser Val Glu Val Lys Lys Val Met Ala Cys Pro Arg Cys Ile Leu Thr Thr Val Asp Pro Asp Thr Gly Val Ile Asp Arg Lys Gln Pro Leu Asp Thr Leu Lys Ser Tyr Arg Leu Cys Asp Pro Ser Glu Arg Glu Leu Tyr Lys Leu Ser Pro Leu Phe Gly Ile Tyr Tyr Ser Val Glu Lys Ile Gly Ser Leu Arg Val Gly Asp Pro Val Tyr Arg Met Val <210> 32 <211> 208 <212> PRT <213> Homo sapiens <400> 32 Met Glu Leu Arg Ala Ala Leu Val Leu Val Leu Leu Ile Ala Gly

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			35					40					45			
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		50			,		55					60			•	
	Ile	Asp	Thr	Met	Phe	His	Leu	Gln	Pro	Leu	Met	Phe	Leu	Gly	Leu	Phe
	65					70					75					80
	Pro	Leu	Phe	Ala	Val	Phe	Glu	Gly	Leu	His	Leu	Ser	Thr	Ser	Glu	Lys
10					85					90					95	
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			115					120					125			
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		130					135					140				
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	145					150					155					160
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	Ile	Ser	Leu	His	Val	Ala	Leu	Lys	Ala	Leu	His	Ser	Arg	Gly	Asn	Pro
				180					185					190		
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			35					40					45			
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		50					55					60				
	Ser	Ile	Thr	Leu	Leu	Gly	Leu	Ala	Val	Asn	Val	Val	Thr	Thr	Leu	Val
15	65	٠				70					75					80
	Leu	Ile	Ser	Tyr	Cys	Pro	Thr	Ala	Thr	Glu	Glu	Ala	Pro	Tyr	Trp	Thr
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	Tyr	Leu	Leu	Cys	Ala	Leu	Gly	Leu	Phe	Ile	Tyr	Gln	Ser	Leu	Asp	Ala
				100					105					110		
20	Ile	Asp	Gly	Lys	Gln	Ala	Arg	Arg	Thr	Asn	Ser	Cys	Ser	Pro	Leu	Gly
			115					120	•				125			
	Glu	Leu	Phe	Asp	His	Gly	Cys	Asp	Ser	Leu	Ser	Thr	Val	Phe	Met	Ala
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	Val	Gly	Ala	Ser	Ile	Ala	Ala	Arg	Leu	Gly	Thr	Tyr	Pro	Asp	Trp	Phe
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	Phe	Phe	Cys	Ser	Phe	Ile	Gly	Met	Phe	Val	Phe	Tyr	Cys	Ala	His	Tr
					165					170					175	
	Gln	Thr	Tyr	Val	Ser	Gly	Met	Leu	Arg	Phe	Gly	Lys	Val	Asp	Val	Thi
				180					185					190		
5	Glu	Ile	Gln	Ile	Ala	Leu	Val	Ile	Val	Phe	Val	Leu	Ser	Ala	Phe	Gl
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	Gly	Ala	Thr	Met	Trp	Asp	Tyr	Thr	Ile	Pro	Ile	Leu	Glu	Ile	Lys	Lev
		210					215					220				
	Lys	Ile	Leu	Pro	Val	Leu	Gly	Phe	Leu	Gly	Gly	Val	Ile	Phe	Ser	Cys
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	Ser	Asn	Tyr	Phe	His	Val	Ile	Leu	His	Gly	Gly	Val	Gly	Lys	Asn	Gly
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	Val	Asn	Trp	Lys	Gly	Ala	Leu	Gly	Gly	Leu	Leu	Thr	Gly	Ile	Thr	Leu
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10	Thr	Thr	Thr	Pro	Gly	Met	Val	Ser	Thr	Asn	Met	Thr	Ser	Thr	Thr	Leu
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	Lys	Ser	Thr	Pro	Lys	Thr	Thr	Ser	Val	Ser	Gln	Asn	Thr	Ser	Gln	Ile
			115					120					125			
	Ser	Thr	Ser	Thr	Met	Thr	Val	Thr	His	Asn	Ser	Ser	Val	Thr	Ser	Ala
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	Ala	Ser	Ser	Val	Thr	Ile	Thr	Thr	Thr	Met	His	Ser	Glu	Ala	Lys	Lys
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	Cys	Gly	Ser	Asp	Cys	Ile	Arg	His	Lys	Gly	Thr	Val	Val	Leu	Cys	Pro
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	Gln	Thr	Gly	Val	Pro	Phe	Pro	Leu	Asp	Asn	Asn	Lys	Ser	Lys	Pro	Gly
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	145					150					155					160	
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,	Ser	Asp	Val	Met	Leu	Lys	Glu	Gly	Tyr	Glu	Asn	Phe	Phe	Asp	Lys	Leu	
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20	Thr			Ile	Phe											
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	505									•						
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23	<b>~</b> 21	2> D	WA.													

### 95 / 346

<213> Homo sapiens .

<400> 41

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<211> 627

<212> DNA

<213> Homo sapiens

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### 96/346

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<212> DNA

<213> Homo sapiens

<400> 43

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### 97 /346

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25

<210> 44

<211> 1857

<212> DNA

<213> Homo sapiens

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5

10

15

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### 99/346

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<210> 45

<211> 627

5 <212> DNA

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15

<213> Homo sapiens

<400> 45

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<211> 1509

<212> DNA

<213> Homo sapiens

<400> 46

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#### 101/346

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<211> 1011

<212> DNA

5 <213> Homo sapiens

<400> 47

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25 <210> 48

### 102/346

<211> 1023

<212> DNA

<213> Homo sapiens

<400> 48

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25 <211> 672

### 103/346

<212> DNA

<213> Homo sapiens

<400> 49

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<212> DNA

20 <213> Homo sapiens

<400> 50

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#### 104/346

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<210> 51

15 <211> 1617

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<212> DNA

<213> Homo sapiens

<220>

<221> CDS

20 <222> (255)..(1262)

<400> 51

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108/346

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Leu Gln Pro Leu Met Phe Leu Gly Leu Phe Pro Leu Phe Ala Val Phe

25

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5	aca	ggg	ctg	ctc	ctg	cgg	gta	ctt	ggg	agc	ctc	ttc	ctt	ggc	ggg	att	512
	Thr	Gly	Leu	Leu	Leu	Arg	Val	Leu	Gly	Ser	Leu	Phe	Leu	Gly	Gly	Ile	
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	Leu	Ala	Phe	Gly	Leu	Gly	Phe	Ser	Glu	Phe	Leu	Leu	Val	Ser	Arg	Thr	•
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	Trp	Leu	Gly	Phe	Ala	Leu	Cys	Leu	Ser	Gly	Ile	Ser	Leu	His	Val	Ala	
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	Leu	Lys	Ala	Leu	His	Ser	Arg	Gly	Asn	Pro	Glu	Ser	Leu	Pro	Glu	Ala	
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<220>

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<222> (60)..(1280)

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	Met	Ala	Ala	Gly	Ala	Gly	Ala	Gly	Ser	Ala	Pro	Arg	Trp	Leu	Arg	Ala	
	1				5					10					15		
5	ctg	agc	gag	ccg	ctg	agc	gcg	gcg	cag	ctg	cgg	cga	ctg	gag	gag	cac	155
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	Leu	Ile	Ser	Tyr	Cys	Pro	Thr	Ala	Thr	Glu	Glu	Ala	Pro	Tyr	Trp	Thr	
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	Ile	Asp	Gly	Lys	Gln	Ala	Arg	Arg	Thr	Asn	Ser	Cys	Ser	Pro	Leu	Gly	
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				Met												-	,,,
	<b>4-</b> 1	210				·wp	215	****	110	110	116	220	Giu	116	пуз	Deu	
	nee		c++	сса	att	c++		+++	at a	aat	~~~		2+2	***	+	Last	770
20																_	779
20		TTG	шеu	Pro	Val		GIĀ	rne	ren	стА		vaı	TTE	Pne	ser		
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	Val	Phe	Glu	Lys	His	Pro	Cys	Leu	Tyr	Ile	Leu	Met	Phe	Gly	Cys	Val	
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	Leu	Cys	Leu	Gln	lle	Ser	Arg	His	Leu	His	Let	ı Asr	ıle	e Phe	Lys	Thr	
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385 390 395 400

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405

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<220>

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gccaatacca ccaccagatt cttcttgaa gtcaactttt gagatettea ctaagtacae 180

gttggtgtct gaagattcac acgagtgcct ctggtaatca ttttcttcag ggaatcacag 240

tctctcctct cagcaaagca tccactgtac tgaactttgc ttttggaaac atcttctcc 300

tgagacctcg ttgaaagaaa ctctctggtg tcatactttc caat atg gag gtg aag 356

Met Glu Val Lys

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25 Asn Phe Ala Val Trp Asp Tyr Val Val Phe Ala Ala Leu Phe Phe Ile

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	Thr	Ser	Arg	Glu	Phe	Leu	Val	Gly	Gly	Arg	Gln	Met	Ser	Phe	Gly	Pro	
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	550					555					560					
	agt ggg	aca	gag	cag	gaa	aac	ctt	gag	aat	ggc	agt	gcc	cgg	aaa	cag	2084
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	His Val	Pro	Gly	Tyr	Asp	Pro	Lys	Asp	Lys	Ser	Tyr	Asn	Asn	Met	Ala	
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	taactac	atg (	caaaa	atgad	ct gi	tctc	tcgg	g ata	attci	tttg	aaa	gact	cca a	actt <sup>.</sup>	tcacag	2408
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	D															

25 <213> Homo sapiens

# 120/346

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	Leu	Pro	His	Asn	Ser	Ser	Ala	Asn	Ser	Thr	Glu	Thr	Leu	Gln	His	Val	
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25

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	Met	Thr	Ser	Thr	Thr	Leu	Lys	Ser	Thr	Pro	Lys	Thr	Thr	Ser	Val	Ser	
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	Gln	Asn	Thr	Ser	Gln	Ile	Ser	Thr	Ser	Thr	Met	Thr	Val	Thr	His	Asn	
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	His	Ser	Glu	Ala	Lys	Lys	Gly	Ser	Lys	Phe	Asp	Thr	Gly	Ser	Phe	Val	
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	Cys	Lys	Met	Tyr	Tyr	Ser	Arg	Arg	Gly	Ile	Arg	Tyr	Arg	Thr	Ile	Asp	
20				190					195					200			
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	Glu	His	Asp	Ala	Ile	Ile											
			205														
	caga	attg	atg (	ctgc	cctat	tc aa	atta	attti	t gg1	tta	ttaa	tag	ttta	aaa (	caata	attctc	855
25	ttt	ttga	aaa i	tagt	ataaa	ac a	ggcc	atgc	a tai	taat	gtac	agt	gtat	tac	gtaaa	atatgt	915

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10

15

20

25

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	Ala	Leu	Cys	Arg	Ser	Ala	Val	Pro	Arg	Glu	Pro	Thr	Val	Gln	Cys	Gly	٠.
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	Ala	Asp	Ala	Ser	Ile	Arg	Leu	Leu	Lys	Ala	Thr	Lys	Ile	Cys	Val	Thr	
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	gag	gcc	ttc	cag	act	cag	acc	aga	ccc	tct	ggt	ggt	aaa	tgg	aca	ttt	388
	Glu	Ala	Phe	Gln	Thr	Gln	Thr	Arg	Pro	Ser	Gly	Gly	Lys	Trp	Thr	Phe	
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25 Ser Tyr Ile Gly Phe Pro Val Glu Leu Asn Thr Val Tyr Phe Ile Gly

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	Ala	His	Asn	Ile	Pro	Asn	Ala	Asn	Met	Asn	Glu	Asp	Gly	Pro	Ser	Met	
			140					145					150				
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	Ala	Cys	Lys	Lys	Asn	Glu	Glu	Thr	Val	Glu	Val	Asn	Phe	Thr	Thr	Thr	
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#### 131/346

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	105		110					115					120	
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	Ile Pro	Gly Asn	His Gl	y Asn	Asn	Gly	Asn	Asn	Gly	Ala	Thr	Gly	His	
		140	1			145					150			
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	Glu Gly	_	Gly Gl	u Lys		Asp	Lys	Gly	Asp		Gly	Pro	Arg	
	•	155			160					165				- 4 -
	ggg gag													640
4.5	Gly Glu	Arg Gly	7 Gln Hi			Lys	GTÀ	Glu		GTĀ	Tyr	Pro	GIŸ	
15	170			175		***			180	a+ a	~~~	200	222	600
		cca gaa							•					688
	11e Pro	PIO GII	1 шей GI 19		ALA	Pne	Mec	195		пеп	Ala	1111	200	
		aat ca			att	atc	ttc			att	gag	acc		736
20		Asn Gli												
			205	<u>,</u>			210					215		
	att gga	aac tt		g tca	. tga	.ctgg			gggg	cc c	cagt	atca	.g	78
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	gaagatgaca a	ggcctacca tcgt	tgg gccgtcaggc a	gttggttgg 120						
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					Met Ala					
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	act ctg agt	gtt ata ggt tc	a agt tca ctt a	att gcc tat gct	gta ttc 225					
	Thr Leu Ser	Val Ile Gly Se	er Ser Ser Leu :	Ile Ala Tyr Ala	Val Phe					
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	cat aat ata	cag aaa tct cc	a gag ata aga d	cca ctt ttt tat	ctg agc 273					
	His Asn Ile	Gln Lys Ser Pr	co Glu Ile Arg 1	Pro Leu Phe Tyr	Leu Ser					
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	ttc tgt gac	ctg ctc ctg gg	ga ctt tgc tgg (	ctc acg gag aca	ctt ctc 321					
15	Phe Cys Asp	Leu Leu Leu Gl	y Leu Cys Trp 1	Leu Thr Glu Thr	Leu Leu					
	35	40		45	50					
	tat gga gct	tca gta gca aa	it aag gac atc a	atc tgc tat aac	cta caa 369					
	Tyr Gly Ala	Ser Val Ala As	sn Lys Asp Ile :	Ile Cys Tyr Asn	Leu Gln					
		55	60		65					
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	Ala Val Gly	Gln Ile Phe Ty	r Ile Ser Ser	Phe Leu Tyr Thr	Val Asn					
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	tac atc tgg	tat ttg tac ac	a gag ctg agg a	atg aaa cac acc	cag agt 465					
	Tyr Ile Trp	Tyr Leu Tyr Th	nr Glu Leu Arg I	Met Lys His Thr	Gln Ser					
25	85		90	95						

	ç	gga	cag	agc	aca	tct	cca	ctg	gtg	ata	gat	tat	act	tgt	cga	gtt	tgt	513
	G	Sly	Gln	Ser	Thr	Ser	Pro	Leu	Val	Ile	Asp	Tyr	Thr	Cys	Arg	Val	Cys	
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	c	aa	atg	gcc	ttt	gtt	ttc	tca	agg	tgt	atc	ttg	atg	cac	tca	cca	cca	561
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	t	ca	gcc	atg	gct	gaa	ctt	cca	cct	tct	gcc	aac	aca	tct	gtc	tgt	agc	609
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	7	Chr	Leu	Tyr	Phe	Tyr	Gly	Ile	Ala	Ile	Phe	Leu	Gly	Ser	Phe	Val	Leu	
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	1	Lуs	Lys	Phe	Val	Lys	Ser	Thr	Gly	Phe	Leu	Gly	Ser	Glu	Gln	Trp	Ala	
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20	7	Val	Ile	His	Ile	Val	Asp	Gln	Arg	Val	Arg	Phe	Tyr	Pro	Val	Ala	Phe	
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	1	Phe	Cys	Cys	Trp	Gly	Pro	Ala	Val	Ile	Leu	Met	Ile	Ile	Lys	Leu	Thr	
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	Leu	Thr	Ala	Thr	Ser	Gln	Gly	Leu	Leu	Asn	Cys	Gly	Val	Tyr	Gly	Trp	
5			245					250					255				
	acg	cag	cac	aaa	ttc	cac	caa	cta	aag	cag	gag	gct	cgg	cgt	gat	gca	993
	Thr	Gln	His	Lys	Phe	His	Gln	Leu	Lys	Gln	Glu	Ala	Arg	Arg	Asp	Ala	
		260					265					270					
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10	Asp	Thr	Gln	Thr	Pro	Leu	Leu	Cys	Ser	Gln	Lys	Arg	Phe	Tyr	Ser	Arg	
	275					280					285					290	
	ggc	tta	aat	tca	ctg	gaa	tcc	acc	ctg	act	ttt	cct	gcc	agt	act	tct	1089
	Gly	Leu	Asn	Ser	Leu	Glu	Ser	Thr	Leu	Thr	Phe	Pro	Ala	Ser	Thr	Ser	
					295					300				•	305		
15	acc	att	ttt	tgaa	acta	aca a	atact	ggaa	c at	.ccaç	gaac	tg:	gagtt	att			1138
	Thr	Ile	Phe														
	ctac	gcta	aat g	gatt	ggaa	aa ga	aatgt	tggg	, aaa	ıggac	catc	ttaa	atct	tt 1	tctaa	actatg	1198
	ccct	aaac	ctg d	cagaa	actca	aa ag	gaaa	atata	gto	rccat	tgt	tagt	agto	cat 1	tctag	gatgaa	1258
	ttgg	gagt	at o	ctctc	cagt	t at	tcc	cagat	tca	ctag	gtga	tcct	taaa	agt d	ctcta	attcag	1318
20	ggag	gagga	ag a	acact	ttcc	ca to	ctcaç	gagat	. aga	ctcg	gtgt	taco	ettga	atg q	gatat	tggat	1378
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<213> Homo sapiens

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				20					25					30		
	Ser	Ala	Pro	Val	Leu	Glu	Glu	Gly	Asp	Thr	Asp	Pro	Trp	Thr	Leu	Pro
			35					40					45			
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		50					55					60				
	Arg	Leu	Arg	Arg	Val	Ala	Gly	Ser	Val	Leu	Lys	Ala	Cys	Gly	Leu	Leu
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	Phe	Gln	Leu	Leu	Gly	Ser	Lys	Val	Ala	Gly	Asp	Ile	Phe	Lys	Asp	Asn
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		130					135					140				
	Met	Val	Ala	Ala	Lys	Leu	Leu	Thr	Val	Arg	Val	Ser	Val	Pro	Ile	Ile
	145					150					155					160
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		Ala	Gln	Ser	Gly	Asp	Arg	Asp	Glu	Phe	Gln	Arg	Ala	Phe	Ser	Gly	Ser
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		Ala	Val	His	Gly	Ile	Phe	Asn	Trp	Leu	Thr	Val	Leu	Val	Leu	Leu	Pro
				195					200					205			
	5	Leu	Glu	Ser	Ala	Thr	Ala	Leu	Leu	Glu	Arg	Leu	Ser	Glu	Leu	Ala	Leu
			210					215					220				
		Gly	Ala	Ala	Ser	Leu	Thr	Pro	Arg	Ala	Gln	Ala	Pro	Asp	Ile	Leu	Lys
		225					230					235					240
		Val	Leu	Thr	Lys	Pro	Leu	Thr	His	Leu	Ile	Val	Gln	Leu	Asp	Ser	Asp
·	10					245					250					255	
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					260					265					270		
		Lys	His	Trp	Cys	Gly	Thr	Thr	Gly	Gln	Pro	Thr	Gln	Glu	Asn	Ser	Ser
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	15	Cys	Gly	Ala	Phe	Gly	Pro	Cys	Thr	Glu	Lys	Asn	Ser	Thr	Ala	Pro	Ala
			290					295					300				
		Asp	Arg	Leu	Pro	Cys	Arg	His	Leu	Phe	Ala	Gly	Thr	Glu	Leu	Thr	Asp
		305					310					315					320
		Leu	Ala	Val	Gly	Cys	Ile	Leu	Leu	Ala	Gly	Ser	Leu	Leu	Val	Leu	Cys
	20					325				•	330					335	
		Gly	Cys	Leu	Val	Leu	Ile	Val	Lys	Leu	Leu	Asn	Ser	Val	Leu	Arg	Gly
					340					345					350		
		Arg	Val	Ala	Gln	Val	Val	Arg	Thr	Val	Ile	Asn	Ala	Asp	Phe	Pro	Phe
				355					360					365			
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	Leu	Thr	Phe	Ala	Leu	Gln	Ser	Ser	Ser	Val	Phe	Thr	Ala	Ala	Val	Val
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	Pro	Leu	Met	Gly	Val	Gly	Val	Ile	Ser	Leu	Asp	Arg	Ala	Tyr	Pro	Leu
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	Leu	Leu	Gly	Ser	Asn	Ile	Gly	Thr	Thr	Thr	Thr	Ala	Leu	Leu	Ala	Ala
				420					425					430		
	Leu	Ala	Ser	Pro	Ala	Asp	Arg	Met	Leu	Ser	Ala	Leu	Gln	Val	Ala	Leu
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10	Ile	His	Phe	Phe	Phe	Asn	Leu	Ala	Gly	Ile	Leu	Leu	Trp	Tyr	Leu	Val
		450					455					460				
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				500					505					510		
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			515					520					525			
20	Ile	Leu	Val	Thr	Val	Leu	Gln	Arg	Arg	Arg	Pro	Ala	Trp	Leu	Pro	Val
		530					535					540				
	Arg	Leu	Arg	Ser	Trp	Ala	Trp	Leu	Pro	Val	Trp	Leu	His	Ser	Leu	Glu
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Ile Leu Ala Ser Gln Gln Leu
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Phe Val Ile Leu Leu Phe Ile Phe Leu Gly Ile Leu Ile Val Arg Cys

35 40 45

Phe Arg Ile Leu Leu Asp Pro Tyr Arg Ser Met Pro Thr Ser Thr Trp
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Leu Arg Thr Ser Asp Pro Asp Phe Leu Ala Ala Val Asp Ser Trp Phe

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	Asn	Ile	Ile	Ser	Ile	Gln	Val	Glu	Asn	Glu	Tyr	Gly	Ser	Tyr	Arg	Ala
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			195					200					205			
	Leu	Gly	Glu	Lys	Ile	Leu	Leu	Phe	Thr	Thr	Asp	Gly	Pro	Glu	Gly	Leu
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	His	Gly	Pro	Leu	Val	Asn	Ser	Glu	Tyr	Tyr	Thr	Gly	Trp	Leu	Asp	Tyr
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15	Trp	Gly	Gln	Asn	His	Ser	Thr	Arg	Ser	Val	Ser	Ala	Val	Thr	Lys	Gly
			275					280					285			
	Leu	Glu	Asn	Met	Leu	Lys	Leu	Gly	Ala	Ser	Val	Asn	Met	Tyr	Met	Phe
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					325					330					335	
	Glu	Ala	Gly	Asp	Pro	Thr	Pro	Lys	Leu	Phe	Ala	Leu	Arg	Asp	Val	Ile
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25	Ser	Lys	Phe	Gln	Glu	Va1	Pro	Leu	Glv	Pro	Leu	Pro	Pro	Pro	Ser	Pro

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	Pro	Met	Thr	Phe	Glu	Ala	Val	Lys	Gln	Asp	His	Gly	Phe	Met	Leu	Туг
					405					410					415	
	Arg	Thr	Tyr	Met	Thr	His	Thr	Ile	Phe	Glu	Pro	Thr	Pro	Phe	Trp	Val
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	Leu	Ser	Phe	Gly	Ser	Asn	Ser	Ser	Asp	Phe	Lys	Gly	Leu	Leu	Lys	Pro
					485					490					495	
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				500					505					510		
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	Trp	Thr	Lys	Gln	Gly	Pro	Gln	Gln	Thr	Leu	Tyr	Val	Pro	Arg	Phe	Leu
				580					585					590		
5	Leu	Phe	Pro	Arg	Gly	Ala	Leu	Asn	Lys	Ile	Thr	Leu	Leu	Glu	Leu	Glu
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20	Met	Gly	Met	Asp	Asp	Cys	Asp	Ser	Phe	Phe	Pro	Gly	Pro	Leu	Val	Ala
	1				5					10					15	
	Ile	Ile	Cys	Asp	Ile	Leu	Gly	Glu	Lys	Thr	Thr	Ser	Ile	Leu	Gly	Ala
				20					25					30		
	Phe	Val	Val	Thr	Gly	Gly	Tyr	Leu	Ile	Ser	Ser	Trp	Ala	Thr	Ser	Ile
25			35					40					45			

	Pro	Phe	Leu	Cys	Val	Thr	Met	Gly	Leu	Leu	Pro	Gly	Leu	Gly	Ser	Ala
		50					55					60				
	Phe	Leu	Tyr	Gln	Val	Ala	Ala	Val	Val	Thr	Thr	Lys	Tyr	Phe	Lys	Lys
	65					70					75		•			80
5	Arg	Leu	Ala	Leu	Ser	Thr	Ala	Ile	Ala	Arg	Ser	Gly	Met	Gly	Leu	Thr
					85					90			•		95	
	Phe	Leu	Leu	Ala	Pro	Phe	Thr	Lys	Phe	Leu	Ile	Asp	Leu	Tyr	Asp	Trp
				100					105					110		
	Thr	Gly	Ala	Leu	Ile	Leu	Phe	Gly	Ala	Ile	Ala	Leu	Asn	Leu	Val	Pro
10			115		•			120					125			
	Ser	Ser	Met	Leu	Leu	Arg	Pro	Ile	His	Ile	Lys	Ser	Glu	Asn	Asn	Ser
		130					135					140				
	Gly	Ile	Lys	Asp	Lys	Gly	Ser	Ser	Leu	Ser	Ala	His	Gly	Pro	Glu	Ala
	145					150					155					160
15	His	Alạ	Thr	Glu	Thr	His	Cys	His	Glu	Thr	Glu	Glu	Ser	Thr	Ile	Lys
					165					170					175	
	Asp	Ser	Thr	Thr	Gln	Lys	Ala	Gly	Leu	Pro	Ser	Lys	Asn	Leu	Thr	Val
				180					185					190		
	Ser	Gln	Asn	Gln	Ser	Glu	Glu	Phe	Tyr	Asn	Gly	Pro	Asn	Arg	Asn	Arg
20			195			-		200					205			
	Leu	Leu	Leu	Lys	Ser	Asp	Glu	Glu	Ser	Asp	Lys	Val	'Ile	Ser	Trp	Ser
		210					215					220				
	Cys	Lys	Gln	Leu	Phe	Asp	Ile	Ser	Leu	Phe	Arg	Asn	Pro	Phe	Phe	Tyr
	225					230					235					240
25	Ile	Phe	Thr	Trp	Ser	Phe	Leu	Leu	Ser	Gln	Leu	Ala	Tvr	Phe	Ile	Pro

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					245					250					255	
	Thr	Phe	His	Leu	Val	Ala	Arg	Ala	Lys	Thr	Leu	Gly	Ile	Asp	Ile	Met
				260					265					270		
	Asp	Ala	Ser	Tyr	Leu	Val	Ser	Val	Ala	Gly	Ile	Leu	Glu	Thr	Val	Sei
5			275					280					285			
	Gln	Ile	Ile	Ser	Gly	Trp	Val	Ala	Asp	Gln	Asn	Trp	Ile	Lys	Lys	Туз
		290					295					300				
	His	Tyr	His	Lys	Ser	Tyr	Leu	Ile	Leu	Cys	Gly	Ile	Thr	Asn	Leu	Let
	305					310					315					320
10	Ala	Pro	Leu	Ala	Thr	Thr	Phe	Pro	Leu	Leu	Met	Thr	Tyr	Thr	Ile	Cys
					325					330					335	
	Phe	Ala	Ile	Phe	Ala	Gly	Gly	Tyr	Leu	Ala	Leu	Ile	Leu	Pro	Val	Leu
				340					345					350		
	Val	Asp	Leu	Cys	Arg	Asn	Ser	Thr	Val	Asn	Arg	Phe	Leu	Gly	Leu	Ala
15			355					360					365			
	Ser	Phe	Phe	Ala	Gly	Met	Ala	Val	Leu	Ser	Gly	Pro	Pro	Ile	Ala	Gly
		370		d			375					380				
	Asn	Thr	Phe	Thr	Thr	Phe										
	385					390										
20																
	<210	)> 65	5													
		L> 45														
	<212	?> PF	T													
	<213	3> Hc	mo s	sapie	ens											

25

	<400	)> 65	•													
	Met	Glu	Leu	Ala	Leu	Arg	Arg	Ser	Pro	Val	Pro	Arg	Trp	Leu	Leu	Leu
	1				5					10					15	
	Leu	Pro	Leu	Leu	Leu	Gly	Leu	Asn	Ala	Gly	Ala	Val	Ile	Asp	Trp	Pro
5				20					25					30		
	Thr	Glu	Glu	Gly	Lys	Glu	Val	Trp	Asp	Tyr	Val	Thr	Val	Arg	Lys	Asp
			35					40					45			
	Ala	Tyr	Met	Phe	Trp	Trp	Leu	Tyr	Tyr	Ala	Thr	Asn	Ser	Cys	Lys	Asn
		50					55					60				
10	Phe	Ser	Glu	Leu	Pro	Leu	Val	Met	Trp	Leu	Gln	Gly	Gly	Pro	Gly	Gly
	65					70					75					80
	Ser	Ser	Thr	Gly	Phe	Gly	Asn	Phe	Glu	Glu	Ile	Gly	Pro	Leu	Asp	Ser
					85					90					95	
	Asp	Leu	Lys	Pro	Arg	Lys	Thr	Thr	Trp	Leu	Gln	Ala	Ala	Ser	Leu	Leu
15				100					105					110		
	Phe	Val	Asp	Asn	Pro	Val	Gly	Thr	Gly	Phe	Ser	Tyr	Val	Asn	Gly	Ser
			115					120					125			
	Gly	Ala	Tyr	Ala	Lys	Asp	Leu	Ala	Met	Val	Ala	Ser	Asp	Met	Met	Val
		130	1				135					140				
20	Leu	Leu	Lys	Thr	Phe	Phe	Ser	Cys	His	Lys	Glu	Phe	Gln	Thr	Val	Pro
	145	•				150	)				155					160
	Phe	Tyr	: Ile	Phe	Ser	Glu	Ser	Tyr	Gly	Gly	' Lys	Met	Ala	Ala	Gly	Ile
					165	<b>j</b>				170	)				175	
	Gly	Leu	ı Glu	ı Lev	Туг	Lys	s Ala	Ile	Glr	Arg	d GJ7	Thr	: Ile	Lys	Cys	Asn
25				180	)				185	j				190	1	

	Phe	Ala	Gly	Val	Ala	Leu	Gly	Asp	Ser	Trp	Ile	Ser	Pro	Val	Asp	Ser
			195					200					205			
	Val	Leu	Ser	Trp	Gly	Pro	Tyr	Leu	Tyr	Ser	Met	Ser	Leu	Leu	Glu	Asp
		210					215					220				
5	Lys	Gly	Leu	Ala	Glu	Val	Ser	Lys	Val	Ala	Glu	Gln	Val	Leu	Asn	Ala
	225					230					235					240
	Val	Asn	Lys	Gly	Leu	Tyr	Arg	Glu	Ala	Thr	Glu	Leu	Trp	Gly	Lys	Ala
					245					250					255	
	Glu	Met	Ile	Ile	Glu	Gln	Asn	Thr	Asp	Gly	Val	Asn	Phe	Tyr	Asn	Ile
10				260					265		٠			270		
	Leu	Thr	Lys	Ser	Thr	Pro	Thr	Ser	Thr	Met	Glu	Ser	Ser	Leu	Glu	Phe
			275					280					285			
	Thr	Gln	Ser	His	Leu	۷al	Суз	Leu	Cys	Gln	Arg	His	Val	Arg	His	Leu
		290					295					300				
15	Gln	Arg	Asp	Ala	Leu	Ser	Gln	Leu	Met	Asn	Gly	Pro	Ile	Arg	Lys	Lys
	305					310					315					320
	Leu	Lys	Ile	Ile	Pro	Glu	Asp	Gln	Ser	Trp	Gly	Gly	Gln	Ala	Thr	Asn
					325					330					335	
	Val	Phe	Val	Asn	Met	Glu	Glu	Asp	Phe	Met	Lys	Pro	Val	Ile	Ser	Ile
20				340					345					350		
	Val	Asp	Glu	Leu	Leu	Glu	Ala	Gly	Ile	Asn	Val	Thr	Val	Tyr	Asn	Gly
			355					360					365			
	Gln	Leu	Asp	Leu	Ile	Val	Asp	Thr	Met	Gly	Gln	Glu	Ala	Trp	Val	Arg
		370					375					380				
25	Lys	Leu	Lys	Trp	Pro	Glu	Leu	Pro	Lys	Phe	Ser	Gln	Leu	Lys	Trp	Lys

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Ala Leu Tyr Ser Asp Pro Lys Ser Leu Glu Thr Ser Ala Phe Val Lys Ser Tyr Lys Asn Leu Ala Phe Tyr Trp Ile Leu Lys Ala Gly His Met Val Pro Ser Asp Gln Gly Asp Met Ala Leu Lys Met Met Arg Leu Val Thr Gln Gln Glu <210> 66 <211> 490 <212> PRT <213> Homo sapiens <400> 66 Met Arg Pro Ala Phe Ala Leu Cys Leu Leu Trp Gln Ala Leu Trp Pro Gly Pro Gly Gly Glu His Pro Thr Ala Asp Arg Ala Gly Cys Ser Ala Ser Gly Ala Cys Tyr Ser Leu His His Ala Thr Met Lys Arg Gln Ala Ala Glu Glu Ala Cys Ile Leu Arg Gly Gly Ala Leu Ser Thr Val Arg Ala Gly Ala Glu Leu Arg Ala Val Leu Ala Leu Leu Arg Ala Gly

	65					70					75					80
	Pro	Gly	Pro	Gly	Gly	Gly	Ser	Lys	Asp	Leu	Leu	Phe	Trp	Val	Ala	Leu
					85					90					95	
	Glu	Arg	Arg	Arg	Ser	His	Cys	Thr	Leu	Glu	Asn	Glu	Pro	Leu	Arg	Gly
5				100					105					110		
	Phe	Ser	Trp	Leu	Ser	Ser	Asp	Pro	Gly	Gly	Leu	Glu	Ser	Asp	Thr	Leu
			115					120					125			
	Gln	Trp	Val	Glu	Glu	Pro	Gln	Arg	Ser	Cys	Thr	Ala	Arg	Arg	Cys	Ala
		130					135					140				
10	· Val	Leu	Gln	Ala	Thr	Gly	Gly	Val	Glu	Pro	Ala	Gly	Trp	Ьуs	Glu	Met
	145					150					155					160
	Arg	Cys	His	Leu	Arg	Ala	Asn	Gly	Tyr	Leu	Cys	Lys	Tyr	Gln	Phe	Glu
					165					170					175	
	Val	Leu	Cys	Pro	Ala	Pro	Arg	Pro	Gly	Ala	Ala	Ser	Asn	Leu	Ser	Tyr
15				180					185					190		
	Arg	Ala	Pro	Phe	Gln	Leu	His	Ser	Ala	Ala	Leu	Asp	Phe	Ser	Pro	Pro
			195					200					205			
	Gly	Thr	Glu	Val	Ser	Ala	Leu	Cys	Arg	Gly	Gln	Leu	Pro	Ile	Ser	Val
		210					215					220				
20	Thr	Cys	Ile	Ala	Asp	Glu	Ile	Gly	Ala	Arg	Trp	Asp	Lys	Leu	Ser	Gly
	225					230					235					240
	Asp	Val	Leu	Cys	Pro	Cys	Pro	Gly	Arg	Tyr	Leu	Arg	Ala	Gly	Lys	Cys
					245					250					255	
	Ala	Glu	Leu	Pro	Asn	Cys	Leu	Asp	Asp	Leu	Gly	Gly	Phe	Ala	Cys	Glu
25				260					265					270		

	Cys	Ala	Thr	Gly	Phe	Glu	Leu	Gly	Lys	Asp	Gly	Arg	Ser	Cys	Val	Thr
			275					280					285			
	Ser	Gly	Glu	Gly	Gln	Pro	Thr	Leu	Gly	Gly	Thr	Gly	Val	Pro	Thr	Arg
		290					295					300				
5	Arg	Pro	Pro	Ala	Thr	Ala	Thr	Ser	Pro	Val	Pro	Gln	Arg	Thr	Trp	Pro
	305					310					315					320
	Ile	Arg	Val	Asp	Glu	Lys	Leu	Gly	Gļu	Thr	Pro	Leu	Val	Pro	Glu	Gln
					325					330					335	
	Asp	Asn	Ser	Val	Thr	Ser	Ile	Pro	Glu	Ile	Pro	Arg	Trp	Gly	Ser	Gln
10				340				*	345					350		
	Ser	Thr	Met	Ser	Thr	Leu	Gln	Met	Ser	Leu	Gln	Ala	Glu	Ser	Lys	Ala
			355					360					365			
	Thr	Ile	Thr	Pro	Ser	Gly	Ser	Val	Ile	Ser	Lys	Phe	Asn	Ser	Thr	Thr
		370					375					380				
15	Ser	Ser	Ala	Thr	Pro	Gln	Ala	Phe	Asp	Ser	Ser	Ser	Ala	Val	Val	Phe
	385					390					395					400
	Ile	Phe	Val	Ser	Thr	Ala	Val	۷al	Val	Leu	Val	Íle	Leu	Thr	Met	Thr
					405					410					415	
	Val	Leu	Gly	Leu	Val	Lys	Leu	Cys	Phe	His	Glu	Ser	Pro	Ser	Ser	Gln
20				420					425					430		
	Pro	Arg	Lys	Glu	Ser	Met	Gly	Pro	Pro	Gly	Leu	Glu	Ser	Asp	Pro	Glu
			435					440					445			
	Pro	Ala	Ala	Leu	Gly	Ser	Ser	Ser	Ala	His	Суз	Thr	Asn	Asn	Gly	Val
		450					455					460				
25	Lys	Val	Gly	Asp	Cys	Asp	Leu	Arg	Asp	Ara	Ala	Glu	Glv	Ala	Leu	Leu

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Ala Glu Ser Pro Leu Gly Ser Ser Asp Ala .490 <210> 67 <211> 392 <212> PRT <213> Homo sapiens <400> 67 Met Gln Val Asn Thr Thr Lys Phe Met Leu Leu Tyr Ala Trp Tyr Ser Trp Pro Asn Val Val Leu Cys Phe Phe Gly Gly Phe Leu Ile Asp Arg Val Phe Gly Ile Arg Trp Gly Thr Ile Ile Phe Ser Cys Phe Val Cys Ile Gly Gln Val Val Phe Ala Leu Gly Gly Ile Phe Asn Ala Phe Trp Leu Met Glu Phe Gly Arg Phe Val Phe Gly Ile Gly Gly Glu Ser Leu Ala Val Ala Gln Asn Thr Tyr Ala Val Ser Trp Phe Lys Gly Lys Glu Leu Asn Leu Val Phe Gly Leu Gln Leu Ser Met Ala Arg Ile Gly Ser Thr Val Asn Met Asn Leu Met Gly Trp Leu Tyr Ser Lys Ile Glu Ala

			115					120					125			
	Leu	Leu	Gly	Ser	Ala	Gly	His	Thr	Thr	Leu	Gly	Ile	Thr	Leu	Met	Ile
		130					135					140				
	Gly	Gly	Ile	Thr	Cys	Ile	Leu	Ser	Leu	Ile	Cys	Ala	Leu	Ala	Leu	Ala
5	145					150					155					160
	Tyr	Leu	Asp	Gln	Arg	Ala	Glu	Arg	Ile	Leu	His	Lys	Glu	Gln	Gly	Lys
					165					170					175	
	Thr	Gly	Glu	Val	Ile	Lys	Leu	Thr	Asp	Val	Lys	Asp	Phe	Ser	Leu	Pro
				180					185					190		
10	Leu	Trp	Leu	Ile	Phe	Ile	Ile	Cys	Val	Cys	Tyr	Tyr	Val	Ala	Val	Phe
			195					200					205			
	Pro	Phe	Ile	Gly	Leu	Gly	Lys	Val	Phe	Phe	Thr	Glu	Lys	Phe	Gly	Phe
		210					215					220				
	Ser	Ser	Gln	 Ala	Ala	Ser	Ala	Ile	Asn	Ser	Val	Val	Tyr	Val	Ile	Ser
15	225					230					235					240
	Ala	Pro	Met	Ser	Pro	۷al	Phe	Gly	Leu	Leu	Val	Asp	Lys	Thr	Gly	Lys
					245					250					255	
	Asn	Ile	Ile	Trp	Val	Leu	Cys	Ala	Val	Ala	Ala	Thr	Leu	Val	Ser	His
				260					265					270		
20	Met	Met	Leu	Ala	Phe	Thr	Met	Trp	Asn	Pro	Trp	Ile	Ala	Met	Cys	Leu
			275					280					285			
	Leu	Gly	Leu	Ser	Tyr	Ser	Leu	Leu	Ala	Cys	Ala	Leu	Trp	Pro	Met	Val
		290					295					300				
	Ala	Phe	Val	Val	Pro	Glu	His	Gln	Leu	Gly	Thr	Ala	Tyr	Gly	Phe	Met
25	305					310					315					320

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Gln Ser Ile Gln Asn Leu Gly Leu Ala Ile Ile Ser Ile Ile Ala Gly Met Ile Leu Asp Ser Arg Gly Tyr Leu Phe Leu Glu Val Phe Phe Ile Ala Cys Val Ser Leu Ser Leu Ser Val Val Leu Leu Tyr Leu Val Asn Arg Ala Gln Gly Gly Asn Leu Asn Tyr Ser Ala Arg Gln Arg Glu Glu Ile Lys Phe Ser His Thr Glu <210> 68 <211> 538 <212> PRT <213> Homo sapiens <400> 68 Met Gly Cys Leu Trp Gly Leu Ala Leu Pro Leu Phe Phe Cys Trp Glu Val Gly Val Ser Gly Ser Ser Ala Gly Pro Ser Thr Arg Arg Ala Asp Thr Ala Met Thr Thr Asp Asp Thr Glu Val Pro Ala Met Thr Leu Ala Pro Gly His Ala Ala Leu Glu Thr Gln Thr Leu Ser Ala Glu Thr

	Ser	Ser	Arg	Ala	Ser	Thr	Pro	Ala	Gly	Pro	Ile	Pro	Glu	Ala	Glu	Thr
	65					70					75					80
	Arg	Gly	Ala	Lys	Arg	Ile	Ser	Pro	Ala	Arg	Glu	Thr	Arg	Ser	Phe	Thr
					85					90					95	
5	Lys	Thr	Ser	Pro	Asn	Phe	Met	Val	Leu	Ile	Ala	Thr	Ser	Val	Glu	Thr
				100					105					110		
	Ser	Ala	Ala	Ser	Gly	Ser	Pro	Glu	Gly	Ala	Gly	Met	Thr	Thr	Val	Gln
			115					120					125			
	Thr	Ile	Thr	Gly	Ser	Asp	Pro	Glu	Glu	Ala	Ile	Phe	Asp	Thr	Leu	Cys
10		130					135					140				
	Thr	Asp	Asp	Ser	Ser	Glu	Glu	Ala	Lys	Thr	Leu	Thr	Met	Asp	Ile	Leu
	145					150					155					160
	Thr	Leu	Ala	His	Thr	Ser	Thr	Glu	Ala	Lys	Gly	Leu	Ser	Ser	Glu	Ser
					165					170					175	
15	Ser	Ala	Ser	Ser	Asp	Gly	Pro	His	Pro	Val	Ile	Thr	Pro	Ser	Arg	Ala
				180					185					190		
	Ser	Glu	Ser	Ser	Ala	Ser	Ser	Asp	Gly	Pro	His	Pro	Val	Ile	Thr	Pro
			195					200					205			
	Ser	Arg	Ala	Ser	Glu	Ser	Ser	Ala	Ser	Ser	Asp	Gly	Pro	His	Pro	Val
20		210					215					220				
	Ile	Thr	Pro	Ser	Trp	Ser	Pro	Gly	Ser	Asp	Val	Thr	Leu	Leu	Ala	Glu
	225	;				230					235					240
	Ala	Leu	Val	Thr	Val	Thr	Asn	Ile	Glu	Val	Ile	Asn	Cys	Ser	Ile	Thr
					245					250					255	
25	Glu	ı Ile	Glu	Thr	Thr	Thr	Ser	Ser	Ile	Pro	Gly	Ala	Ser	Asp	Ile	Asp

				260					265					270		
	Leu	Ile	Pro	Thr	Glu	Gly	Val	Lys	Ala	Ser	Ser	Thr	Ser	Asp	Pro	Pro
			275					280					285			
	Ala	Leu	Pro	Asp	Ser	Thr	Glu	Ala	Lys	Pro	His	Ile	Thr	Glu	۷al	Thr
5		290					295					300				
	Ala	Ser	Ala	Glu	Thr	Leu	Ser	Thr	Ala	Gly	Thr	Thr	Glu	Ser	Ala	Ala
	305					310					315					320
	Pro	His	Ala	Thr	Val	Gly	Thr	Pro	Leu	Pro	Thr	Asn	Ser	Ala	Thr	Glu
					325					330					335	
10	Arg	Glu	Val	Thr	Ala	Pro	Gly	Ala	Thr	Thr	Leu	Ser	Gly	Ala	Leu	Val
				340					345					350		
	Thr	Val	Ser	Arg	Asn	Pro	Leu	Glu	Glu	Thr	Ser	Ala	Leu	Ser	Val	Glu
			355					360					365			
	Thr	Pro	Ser	Tyr	Val	Lys	Val	Ser	Gly	Ala	Ala	Pro	Val	Ser	Ile	Glu
15		370					375					380			•	
	Ala	Gly	Ser	Ala	Val	Gly	Lys	Thr	Thr	Ser	Phe	Ala	Gly	Ser	Ser	Ala
	385					390					395					400
	Ser	Ser	Tyr	Ser	Pro	Ser	Glu	Ala	Ala	Leu	Lys	Asn	Phe	Thr	Pro	Ser
					405					410					415	
20	Glu	Thr	Pro	Thr	Met	Asp	Ile	Ala	Thr	Lys	Gly	Pro	Phe	Pro	Thr	Ser
				420					425					430		
	Arg	Asp	Pro	Leu	Pro	Ser	Val	Pro	Pro	Thr	Thr	Thr	Asn	Ser	Ser	Arg
			435					440					445			
	Gly	Thr	Asn	Ser	Thr	Leu	Ala	Lys	Ile	Thr	Thr	Ser	Ala	Lys	Thr	Thr
25		450					455					460				

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Met Lys Pro Pro Thr Ala Thr Pro Thr Thr Ala Arg Thr Arg Pro Thr Thr Asp Val Ser Ala Gly Glu Asn Gly Gly Phe Leu Leu Leu Arg Leu Ser Val Ala Ser Pro Glu Asp Leu Thr Asp Pro Arg Val Ala Glu Arg Leu Met Gln Gln Leu His Arg Glu Leu His Ala His Ala Pro His Phe Gln Val Ser Leu Leu Arg Val Arg Arg Gly <210> 69 <211> 102 <212> PRT <213> Homo sapiens <400> 69 Met Glu Ala Ala Leu Leu Gly Leu Cys Asn Trp Ser Thr Leu Gly Val Cys Ala Ala Leu Lys Leu Pro Gln Ile Ser Ala Val Leu Ala Ala Arg Ser Ala Arg Gly Leu Ser Leu Pro Ser Leu Leu Leu Glu Leu Ala Gly Phe Leu Val Phe Leu Arg Tyr Gln Cys Tyr Tyr Gly Tyr Pro Pro Leu 

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Thr Tyr Leu Glu Tyr Pro Ile Leu Ile Ala Gln Asp Val Ile Leu Leu Leu Cys Ile Phe His Phe Asn Gly Asn Val Lys Gln Ala Thr Pro Tyr Ile Ala Val Tyr Pro Phe <210> 70 <211> 442 <212> PRT <213> Homo sapiens <400> 70 Met Gly Leu Ala Met Glu His Gly Gly Ser Tyr Ala Arg Ala Gly Gly Ser Ser Arg Gly Cys Trp Tyr Tyr Leu Arg Tyr Phe Phe Leu Phe Val Ser Leu Ile Gln Phe Leu Ile Ile Leu Gly Leu Val Leu Phe Met Val Tyr Gly Asn Val His Val Ser Thr Glu Ser Asn Leu Gln Ala Thr Glu Arg Arg Ala Glu Gly Leu Tyr Ser Gln Leu Leu Gly Leu Thr Ala Ser Gln Ser Asn Leu Thr Lys Glu Leu Asn Phe Thr Thr Arg Ala Lys Asp 

	Ala	Ile	Met	Gln	Met	Trp	Leu	Asn	Ala	Arg	Arg	Asp	Leu	Asp	Arg	Ile
				100					105					110		
	Asn	Ala	Ser	Phe	Arg	Gln	Cys	Gln	Gly	Asp	Arg	Val	Ile	Tyr	Thr	Asn
			115					120					125			
5	Asn	Gln	Arg	Tyr	Met	Ala	Ala	Ile	Ile	Leu	Ser	Glu	Lys	Gln	Cys	Arg
		130					135					140				
	Asp	Gln	Phe	Lys	Asp	Met	Asn	Lys	Ser	Cys	Asp	Ala	Leu	Leu	Phe	Met
	145					150					155					160
	Leu	Asn	Gln	Lys	Val	Lys	Thr	Leu	Glu	Val	Glu	Ile	Ala	Lys	Glu	Lys
.0					165					170					175	
	Thr	Ile	Cys	Thr	Lys	Asp	Lys	Glu	Ser	Val	Leu	Leu	Asn	Lys	Arg	Val
				180					185					190		
	Ala	Glu	Glu	Gln	Leu	Val	Glu	Cys	Val	Lys	Thr	Arg	Glu	Leu	Gln	His
			195					200					205			
.5	Gln	Glu	Arg	Gln	Leu	Ala	Lys	Glu	Gln	Leu	Gln	Lys	Val	Gln	Ala	Leu
		210					215					220				
	Cys	Leu	Pro	Leu	Asp	Lys	Asp	Lys	Phe	Glu	Met	Asp	Leu	Arg	Asn	Leu
	225					230					235					240
	Trp	Arg	Asp	Ser	Ile	Ile	Pro	Arg	Ser	Leu	Asp	Asn	Leu	Gly	Tyr	Asn
20					245					250					255	
	Leu	Tyr	His	Pro	Leu	Gly	Ser	Glu	Leu	Ala	Ser	Ile	Arg	Arg	Ala	Cys
				260					265					270		
	Asp	His	Met	Pro	Ser	Leu	Met	Ser	Ser	Lys	Val	Glu	Glu	Leu	Ala	Arg
			275					280					285			
25	Ser	Leu	Arg	Ala	Asp	Ile	Glu	Arg	Val	Ala	Arg	Glu	Asn	Ser	Asp	Leu

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G.

		290					295					300				
	Gln	Arg	Gln	Lys	Leu	Glu	Ala	Gln	Gln	Gly	Leu	Arg	Ala	Ser	Gln	Glu
	305					310					315					320
	Ala	Lys	Gln	Lys	Val	Glu	Lys	Glu	Ala	Gln	Ala	Arg	Glu	Ala	Lys	Leu
5					325					330					335	
	Gln	Ala	Glu	Cys	Ser	Arg	Gln	Thr	Gln	Leu	Ala	Leu	Glu	Glu	Lys	Ala
				340					345					350		
	Val	Leu	Arg	Lys	Glu	Arg	Asp	Asn	Leu	Ala	Lys	Glu	Leu	Glu	Glu	Lys
			355					360					365			
10	Lys	Arg	Glu	Ala	Glu	Gln	Leu	Arg	Met	Glu	Leu	Ala	Ile	Arg	Asn	Ser
		370					375					380				
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	385					390					395					400
	Ser	Arg	Pro	Met	Gly	Pro	Val	Pro	Asn	Pro	Gln	Pro	Ile	Asp	Pro	Ala
15					405					410					415	
	Ser	Leu	Glu	Glu	Phe	Lys	Arg	Lys	Ile	Leu	Glu	Ser	Gln	Arg	Pro	Pro
				420					425					430		
	Ala	Gly	Ile	Pro	Val	Ala	Pro	Ser	Ser	Gly						
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20																
	<210	)> 71	L													
	<211	l> 18	300													
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#### 165/346

<400> 71

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#### 166/346

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<211> 246

10 <212> DNA

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<213> Homo sapiens

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ttgggeatte teattgteeg gtgetteegg attettttgg atecatateg aageatgeea 180

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20 <210> 73

<211> 1965

<212> DNA

<213> Homo sapiens

25 <400> 73

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#### 167/346

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### 168/346

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<211> 1173

<212> DNA

<213> Homo sapiens

15 <400> 74

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PCT/JP00/09359 WO 01/49728

### 169/346

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<210> 75

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<211> 1359

<212> DNA

15 <213> Homo sapiens

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20 <213> Homo sapiens

<400> 76

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## 171/346

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### 172/346

<212> DNA

<213> Homo sapiens

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173/346

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<212> DNA

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#### 174/346

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<213> Homo sapiens

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#### 175/346

#### <213> Homo sapiens

<400> 80

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15

20

25

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176/346

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<210> 81

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<400> 81

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His Pro Thr Leu Asp Ala Val Asp Leu Val Glu Lys Thr Leu Arg Asn

15 20 25

gaa ggg acc tcc agt tct gct cca gtc ttg gag gaa ggg gac aca gac 206
Glu Gly Thr Ser Ser Ser Ala Pro Val Leu Glu Gly Asp Thr Asp

30 35 40

ccc tgg acc ctc cct cag ctg aag gac aca agc cag ccc tgg aaa gag 254

Pro Trp Thr Leu Pro Gln Leu Lys Asp Thr Ser Gln Pro Trp Lys Glu

25 45 50 55

	ctc	cgc	gtg	gcc	ggc	agg	ctg	cgc	cgc	gtg	gcc	ggc	agc	gtc	ctc	aag	302
	Leu	Arg	Val	Ala	Gly	Arg	Leu	Arg	Arg	Val	Ala	Gly	Ser	Val	Leu	Lys	
	60			•		65					70					75	
	gcc	tgc	ggg	ctc	ctc	ggc	agc	ctg	tac	ttc	ttc	atc	tgc	tct	ctg	gac	350
5	Ala	Cys	Gly	Leu	Leu	Gly	Ser	Leu	Tyr	Phe	Phe	Ile	Cys	Ser	Leu	Asp	
					80					85					90		
	gtc	ctc	agc	tcc	gcc	ttc	cag	ctg	ctg	ggc	agc	aaa	gtg	gcc	gga	gac	398
	Val	Leu	Ser	Ser	Ala	Phe	Gln	Leu	Leu	Gly	Ser	Lys	۷al	Ala	Gly	Asp	
				95					100					105			
10	atc	ttc	aag	gac	aac	gtg	gtg	ctg	tcc	aac	cct	gtg	gct	gga	ctg	gtc	446
	Ile	Phe	Lys	Asp	Asn	Val	Val	Leu	Ser	Asn	Pro	Val	Ala	Gly	Leu	Val	
			110					115					120				
	att	ggc	gtg	ctg	gtc	aca	gcc	ctg	gtg	cag	agt	tcc	agc	acg	tcc	tcc	494
	Ile	Gly	Val	Leu	Val	Thr	Ala	Leu	Val	Gln	Ser	Ser	Ser	Thr	Ser	Ser	
15		125					130					135					
	tcc	atc	gtg	gtc	agc	atg	gtg	gct	gct	aag	ctg	ctg	act	gtc	cgg	gtg	542
	Ser	Ile	Val	Val	Ser	Met	Val	Ala	Ala	Lys	Leu	Leu	Thr	Val	Arg	Val	
	140					145					150					155	
	tct	gtg	ccc	atc	atc	atg	ggt	gtc	aac	gta	ggc	aca	tcc	atc	acc	agc	590
20	Ser	Val	Pro	Ile	Ile	Met	Gly	Val	Asn	'Val	Gly	Thr	Ser	Ile	Thr	Ser	
					160					165					170		
	acc	ctg	gto	tca	atg	gcg	cag	tca	ggg	gac	cgg	gat	. gaa	ttt	cag	agg	638
	Thr	Leu	Val	. Ser	Met	Ala	Gln	Ser	Gly	Asp	Arg	Asp	Glu	Phe	Gln	Arg	
				175					180					185			
25	gct	ttc	: ago	ggc	tcg	gcg	gtg	cac	ggg	ato	ttc	aac	: tgg	cto	aca	gtg	686

	Ald	Pne	ser	GTĀ	Ser	Ата	vaı	HIS	стА	тте	Pne	Asn	Trp	ьец	ınr	vaı	
			190					195					200				
	ctg	gtc	ctg	ctg	cca	ctg	gag	agc	gcc	acg	gcc	ctg	ctg	gag	agg	cta	734
	Leu	Val	Leu	Leu	Pro	Leu	Glu	Ser	Ala	Thr	Ala	Leu	Leu	Glu	Arg	Leu	
5		205					210					215					
	agt	gag	cta	gcc	ctg	ggt	gcc	gcc	agc	ctg	aca	ccc	agg	gcg	cag	gcg	782
	Ser	Glu	Lẹu	Ala	Leu	Gly	Ala	Ala	Ser	Leu	Thr	Pro	Arg	Ala	Gln	Ala	
	220					225					230					235	
	ccc	gac	atc	ctc	aag	gtg	ctg	acg	aag	ccg	ctc	aca	cac	ctc	atc	gtg	830
10	Pro	Asp	Ile	Leu	Lys	Val	Leu	Thr	Lys	Pro	Leu	Thr	His	Leu	Ile	Val	
					240					245					250		
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	Gln	Leu	Asp	Ser	Asp	Met	Ile	Met	Ser	Ser	Ala	Thr	Gly	Asn	Ala	Thr	
				255					260					265			
15	aac	agc	agt	ctc	att	aag	cac	tgg	tgc	ggc	acc	acg	ggg	cag	ccg	acc	926
	Asn	Ser	Ser	Leu	Ile	Lys	His	Trp	Cys	Gly	Thr	Thr	Gly	Gln	Pro	Thr	4
`			270					275					280				
	cag	gag	aac	agc	agc	tgt	ggc	gcc	ttc	ggc	ccg	tgc	aca	gag	aag	aac	974
	Gln	Glu	Asn	Ser	Ser	Cys	Gly	Ala	Phe	Gly	Pro	Cys	Thr	Glu	Lys	Asn	
20		285					290					295					
	agc	aca	gcc	ccg	gcg	gac	agg	ctg	ccc	tgc	cgc	cac	ctg	ttt	gcg	ggc	1022
	Ser	Thr	Ala	Pro	Ala	Asp	Arg	Leu	Pro	Cys	Arg	His	Leu	Phe	Ala	Gly	
	300					305					310					315	
	acg	gag	ctc	acg	gac	ctg	gcc	gtg	ggc	tgc	atc	ctg	ctg	gcc	ggc	tcc.	1070
25	Thr	Glu	Leu	Thr	Asp	Leu	Ala	Val	Gly	Cys	Ile	Leu	Leu	Ala	Gly	Ser	

		•			320					325					330	•	
	ctg	ctg	gtg	ctc	tgc	ggc	tgc	ctg	gtc	ctc	ata	gtc	aag	ctg	ctc	aac	1118
	Leu	Leu	Val	Leu	Cys	Gly	Cys	Leu	Val	Leu	Ile	Val	Lys	Leu	Leu	Asn	
				335					340					345			
5	tct	gtg	ctg	cgc	ggc	cgc	gtg	gcc	cag	gtc	gtg	agg	aca	gtc	atc	aat	1166
	Ser	Val	Leu	Arg	Gly	Arg	Val	Ala	Gln	Val	Val	Arg	Thr	Val	Ile	Asn	
			350					355					360				
	gcg	gac	ttc	ccc	ttc	ccg	ctg	ggc	tgg	ctc	ggc	ggc	tac	ctg	gcc	gtc	1214
	Ala	Asp	Phe	Pro	Phe	Pro	Leu	Gly	Trp	Leu	Gly	Gly	Tyr	Leu	Ala	Val	
10		365					370					375					
	ctc	gcg	ggc	gcc	ggc	ctg	acc	ttc	gca	ctg	cag	agc	agc	agc	gtc	ttc	1262
	Leu	Ala	Gly	Ala	Gly	Leu	Thr	Phe	Ala	Leu	Gln	Ser	Ser	Ser	Val	Phe	
	380					385					390					395	
	acg	gcg	gcc	gtc	gtg	ccc	ctc	atg	ggg	gtc	ggg	gtg	atc	agt	ctg	gac	1310
15	Thr	Ala	Ala	Val	Val	Pro	Leu	Met	Gly	Val	Gly	Val	Ile	Ser	Leu	Asp	
					400					405					410		
	cgg	gcg	tac	ccc	ctc	tta	ctg	ggc	tcc	aac	atc	ggc	acc	act	acc	aca	1358
	Arg	Ala	Tyr	Pro	Leu	Leu	Leu	Gly	Ser	Asn	Ile	Gly	Thr	Thr	Thr	Thr	
				415					420					425			
20	gcc	ctg	ctg	gct	gcc	ctg	gcc	agc	ccc	gca	gac	agg	atg	ctc	agc	gcc	1406
	Ala	Leu	Leu	Ala	Ala	Leu	Ala	Ser	Pro	Ala	Asp	Arg	Met	Leu	Ser	Ala	
			430					435					440				
	ctg	cag	gtc	gcc	ctc	atc	cac	ttc	ttc	ttc	aac	ctg	gcc	ggc	atc	ctg	1454
	Leu	Gln	Val	Ala	Leu	Ile	His	Phe	Phe	Phe	Asn	Leu	Ala	Gly	Ile	Leu	
25		445					450					455					

	ctg	tgg	tac	ctg	gtg	cct	gca	ctg	cgg	ctg	ccc	atc	ccg	ctg	gcc	agg	1502
	Leu	Trp	Tyr	Leu	Val	Pro	Ala	Leu	Arg	Leu	Pro	Ile	Pro	Leu	Ala	Arg	
	460					465					470					475	
	cac	ttc	ggg	gtg	gtg	acc	gcc	cgt	tac	cgc	tgg	gtg	gct	ggg	gtc	tac	1550
5	His	Phe	Gly	Val	Val	Thr	Ala	Arg	Tyr	Arg	Trp	Val	Ala	Gly	Ϋal	Tyr	
					480					485					490		
	ctg	ctg	ctc	gga	ttc	ctg	ctg	ctg	ccc	ctg	gcg	gcc	ttc	ggg	ctc	tcc	1598
	Leu	Leu	Leu	Gly	Phe	Leu	Leu	Leu	Pro	Leu	Ala	Ala	Phe	Gly	Leu	Ser	
				495					500					505			
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	Leu	Ala	Gly	Gly	Met	Val	Leu	Ala	Ala	Val	Gly	Gly	Pro	Leu	Val	Gly	
			510					515					520				
	ctg	gtg	ctc	ctc	gtc	atc	ctg	gtt	act	gtc	ctg	cag	cgg	cgc	cgg	ccg	1694
	Leu	Val	Leu	Leu	Val	Ile	Leu	Val	Thr	Val	Leu	Gln	Arg	Arg	Arg	Pro	٠
15		525					530					535					
	gcc	tgg	ctg	cct	gtc	cgc	ctg	cgc	tcc	tgg	gcc	tgg	ctc	ccc	gtc	tgg	1742
	Ala	Trp	Leu	Pro	Val	Arg	Leu	Arg	Ser	Trp	Ala	Trp	Leu	Pro	Val	Trp	
	540					545					550					555	
	ctc	cat	tct	ctg	gag	ccc	tgg	gac	cgc	ctg	gtg	acc	cgc	tgc	tgc	ccc	1790
20	Leu	His	Ser	Leu	Glu	Pro	Trp	Asp	Arg	Leu	Val	Thr	Arg	Cys	Cys	Pro	
					560					565					570		
	tgc	aac	gtc	tgc	agc	ccc	ccg	aag	gcc	acc	acc	aaa	gag	gcc	tac	tgc	1838
	Cys	Asn	Val	Cys	Ser	Pro	Pro	Lys	Ala	Thr	Thr	Lys	Glu	Ala	Tyr	Cys	
				575					580					585			
25	tac	gag	aac	cct	gag	atc	ttg	gcc	tcc	cag	cag	ttg	tga	cgg	gcagt	tg	1887

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Tyr Glu Asn Pro Glu Ile Leu Ala Ser Gln Gln Leu

590 595 600

ctgcgcagac cgccccaccc tccccggctg ggagggctct ggagggccct ggagggggg 1947 tccccgcggc agctgacctc cggtcacctg cttccccttc tgtgcaaata aaccaggctg 2007

<210> 82

<211> 1446

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<212> DNA

<213> Homo sapiens

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<220>

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<222> (337)..(582)

15 <400> 82

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gctgggcttc tattaaaatt agactctatt tcctgagcac ccacaaatgg acctgacaaa 180
gggaagacac agatgtactg cgtgatgagg aaagcctatc aggattaaaa tatggctata 240
actcagcctc tccagagtgc agccaccatg acctccgcag attgatgatg gaagaaaaga 300
aaaccaggat atcctgtgct ctggcttccc tggacc atg gat gga gga cag ccc 354
Met Asp Gly Gly Gln Pro

. 5

2016

atc ccc tca tcc cta gtg ccc ctt ggg aac gaa tca gca gat tct agc 402

25 Ile Pro Ser Ser Leu Val Pro Leu Gly Asn Glu Ser Ala Asp Ser Ser

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atg tcc ctg gag cag aaa atg aca ttt gtt ttt gtg att ctg ttg ttt Met Ser Leu Glu Gln Lys Met Thr Phe Val Phe Val Ile Leu Leu Phe att ttc ttg ggc att ctc att gtc cgg tgc ttc cgg att ctt ttg gat Ile Phe Leu Gly Ile Leu Ile Val Arg Cys Phe Arg Ile Leu Leu Asp cca tat cga agc atg cca acc tct acc tgg gct gat gga ctt gaa ggc Pro Tyr Arg Ser Met Pro Thr Ser Thr Trp Ala Asp Gly Leu Glu Gly () · ctg gag aaa ggg cag ttc gac cat gcc ctt gct tag gagggatggt Leu Glu Lys Gly Gln Phe Asp His Ala Leu Ala

75 80

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taggttgcaa gtgcagctta aagtttttt tcaatgaaaa gttaattgtt tagaggagaa 1372 gacttttata gtcttcagag gaatgtgtat ttatgattgt atatagtcac caaataaaac 1432 ttttcaagaa acag 1446

5 <210> 83

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<212> DNA

<213> Homo sapiens

10 <220>

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<222> (40)..(2004)

<400> 83

15 ctgtccgccg tctcagacta gaggagcgct gtaaacgcc atg gct ccc aag aag 54

Met Ala Pro Lys Lys

1 5

ctg tcc tgc ctt cgt tcc ctg ctg ctg ccg ctc agc ctg acg cta ctg 102
Leu Ser Cys Leu Arg Ser Leu Leu Pro Leu Ser Leu Thr Leu Leu

20 10 15 20

ctg ccc cag gca gac act cgg tcg ttc gta gtg gat agg ggt cat gac 150
Leu Pro Gln Ala Asp Thr Arg Ser Phe Val Val Asp Arg Gly His Asp

25 30 35

cgg ttt ctc cta gac ggg gcc ccg ttc cgc tat gtg tct ggc agc ctg 198

25 Arg Phe Leu Leu Asp Gly Ala Pro Phe Arg Tyr Val Ser Gly Ser Leu

			40					45					50				
	cac	tac	ttt	cgg	gta	ccg	cgg	gtg	ctt	tgg	gcc	gac	cgg	ctt	ttg	aag	246
	His	Tyr	Phe	Arg	Val	Pro	Arg	Val	Leu	Trp	Ala	Asp	Arg	Leu	Leu	Lys	
		55					60					65					
5	atg	cga	tgg	agc	ggc	ctc	aac	gcc	ata	cag	ttt	tat	gtg	ccc	tgg	aac	294
	Met	Arg	Trp	Ser	Gly	Leu	Asn	Ala	Ile	Gln	Phe	Tyr	Val	Pro	Trp	Asn	
,	70					75					80					85	
	tac	cac	gag	cca	cag	cct	ggg	gtc	tat.	aac	ttt	aat	ggc	agc	cgg	gac	342
	Tyr	His	Glu	Pro	Gln	Pro	Gly	Val	Tyr	Asn	Phe	Asn	Gly	Ser	Arg	Asp	
10					90					95					100		
	ctc	att	gcc	ttt	ctg	aat	gag	gca	gct	cta	gcg	aac	ctg	ttg	gtc	ata	390
	Leu	Ile	Ala	Phe	Leu	Asn	Glu	Ala	Ala	Leu	Ala	Asn	Leu	Leu	Val	Ile	
				105					110					115			
	ctg	aga	cca	gga	cct	tac	atc	tgt	gca	gag	tgg	gag	atg	ggg	ggt	ctc	438
15	Leu	Arg	Pro	Gly	Pro	Tyr	Ile	Cys	Ala	Glu	Trp	Glu	Met	Gly	Gly	Leu	
			120					125					130				
	cca	tcc	tgg	ttg	ctt	cga	aaa	cct	gaa	att	cat	cta	aga	acc	tca	gat	486
	Pro	Ser	Trp	Leu	Leu	Arg	Lys	Pro	Glu	Ile	His	Leu	Arg	Thr	Ser	Asp	
		135					140					145					
20	cca	gac	ttc	ctt	gcc	gca	gtg	gac	tcc	tgg	ttc	aag	gtc	ttg	ctg	ccc	534
	Pro	Asp	Phe	Leu	Ala	Ala	Val	Asp	Ser	Trp	Phe	Lys	Val	Leu	Leu	Pro	
	150					155					160					165	
	aag	ata	tat	cca	tgg	ctt	tat	cac	aat	ggg	ggc	aac	atc	att	agc	att	582
	Lys	Ile	Tyr	Pro	Trp	Leu	Tyr	His	Asn	Gly	Gly	Asn	Ile	Ile	Ser	Ile	
25					170					175					180		

	cag	gtg	gag	aat	gaa	tat	ggt	agc	tac	aga	gcc	tgt	gac	ttc	agc	tac	630
	Gln	Val	Glu	Asn	Glu	Tyr	Gly	Ser	Tyr	Arg	Ala	Cys	Asp	Phe	Ser	Tyr	
				185					190					195			
	atg	agg	cac	ttg	gct	ggg	ctc	ttc	cgt	gca	ctg	cta	gga	gaa	aag	atc	678
5	Met	Arg	His	Leu	Ala	Gly	Leu	Phe	Arg	Ala	Leu	Leu	Gly	Glu	Lys	Ile	
			200					205					210				
	ttg	ctc	ttc	acc	aca	gat	ggg	cct	gaa	gga	ctc	aag	tgt	ggc	tcc	ctc	726
	Leu	Leu	Phe	Thr	Thr	Asp	Gly	Pro	Glu	Gly	Leu	Lys	Cys	Gly	Ser	Leu	
		215					220					225					
10	cgg	gga	ctc	tat	acc	act	gta	gat	ttt	ggc	сса	gct	gac	aac	atg	acc	774
	Arg	Gly	Leu	Tyr	Thr	Thr	Val	Asp	Phe	Gly	Pro	Ala	Asp	Asn	Met	Thr	
	230					235					240					245	
	aaa	atc	ttt	acc	ctg	ctt	cgg	aag	tat	gaa	ccc	cat	ggg	cca	ttg	gta	822
	Lys	Ile	Phe	Thr	Leu	Leu	Arg	Lys	Tyr	Glu	Pro	His	Gly	Pro	Leu	Val	
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	aac	tct	gag	tac	tac	aca	ggc	tgg	ctg	gat	tac	tgg	ggc	cag	aat	cac	870
	Asn	Ser	Glu	Tyr	Tyr	Thr	Gly	Trp	Leu	Asp	Tyr	Trp	Gly	Gln	Asn	His	
				265					270 <sup>-</sup>					275			
	tcc	aca	cgg	tct	gtg	tca	gct	gta	acc	aaa	gga	cta	gag	aac	atg	'ctc	918
20	Ser	Thr	Arg	Ser	Val	Ser	Ala	Val	Thr	Lys	Gly	Leu	Glu	Asn	Met	Leu	
			280					285					290				
	aag	ttg	gga	gcc	agt	gtg	aac	atg	tac	atg	ttc	cat	gga	ggt	acc	aac	966
	Lys	Leu	Gly	Ala	Ser	Val	Asn	Met	Tyr	Met	Phe	His	Gly	Gly	Thr	Asn	
		295					300			•		305					
25	ttt	gga	tat	tgg	aat	ggt	gcc	gat	aag	aag	gga	cgc	ttc	ctt	ccg	att	101

	Phe	Gly	Tyr	Trp	Asn	Gly	Ala	Asp	Lys	Lys	Gly	Arg	Phe	Leu	Pro	Ile	
	310					315					320					325	
	act	acc	agc	tat	gac	tat	gat	gca	cct	ata	tct	gaa	gca	ggg	gac	ccc	1062
	Thr	Thr	Ser	Tyr	Asp	Tyr	Asp	Ala	Pro	Ile	Ser	Glu	Ala	Gly	Asp	Pro	
5					330					335					340		
	aca	cct	aag	ctt	ttt	gct	ctt	cga	gat	gtc	atc	agc	aag	ttc	cag	gaa	1110
	Thr	Pro	Lys	Leu	Phe	Ala	Leu	Arg	Asp	Val	Ile	Ser	Lys	Phe	Gln	Glu	
				345					350					355			
	gtt	cct	ttg	gga	cct	tta	cct	ccc	ccg	agc	ccc	aag	atg	atg	ctt	gga	1158
10	۷al	Pro	Leu	Gly	Pro	Leu	Pro	Pro	Pro	Ser	Pro	Lys	Met	Met	Leu	Gly	
			360					365					370				
	cct	gtg	act	ctg	cac	ctg	gtt	ggg	cat	tta	ctg	gct	ttc	cta	gac	ttg	1206
	Pro	Val	Thr	Leu	His	Leu	Val	Gly	His	Leu	Leu	Ala	Phe	Leu	Asp	Leu	•
		375					380					385					
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	Leu	Cys	Pro	Arg	Gly	Pro	Ile	His	Ser	Ile	Leu	Pro	Met	Thr	Phe	Glu	
	390					395					400					405	
			aag														1302
	Ala	Val	Lys	Gln	Asp	His	Gly	Phe	Met	Leu	Tyr	Arg	Thr	Tyr	Met	Thr	
20					410					415					420		
•			att														1350
	His	Thr	Ile		Glu	Pro	Thr	Pro	Phe	Trp	Val	Pro	Asn	Asn	Gly	Val	
	٠			425					430					435			
			cgt							•							1398
25	His	Asp	Arg	Ala	Tyr	Val	Met	Val	Asp	Gly	Val	Phe	Gln	Gly	Val	Val	

			440					445					450				
	gag	cga	aat	atg	aga	gac	aaa	cta	ttt	ttg	acg	ggg	aaa	ctg	ggg	tcc	1446
	Glu	Arg	Asn	Met	Arg	Asp	Lys	Leu	Phe	Leu	Thr	Gly	Lys	Leu	Gly	Ser	
		455					460					465					
5	aaa	ctg	gat	atc	ttg	gtg	gag	aac	atg	ggg	agg	ctc	agc	ttt	ggg	tct	1494
	Lys	Leu	Asp	Ile	Leu	Val	Glu	Asn	Met	Gly	Arg	Leu	Ser	Phe	Gly	Ser	
	470					475					480					485	
	aac	agc	agt	gac	ttc	aag	ggc	ctg	ttg	aag	cca	cca	att	ctg	ggg	caa	1542
	Asn	Ser	Ser	Asp	Phe	Lys	Gly	Leu	Leu	Lys	Pro	Pro	Ile	Leu	Gly	Gln	
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	aca	atc	ctt	acc	cag	tgg	atg	atg	ttc	cct	ctg	aaa	att	gat	aac	ctt	1590
	Thr	Ile	Leu	Thr	Gln	Trp	Met	Met	Phe	Pro	Leu	Lys	Ile	Asp	Asn	Leu	
•				505					510					515			
	gtg	aag	tgg	tgg	ttt	ccc	ctc	cag	ttg	cca	aaa	tgg	сса	tat	cct	caa	1638
15	Val	Lys	Trp	Trp	Phe	Pro	Leu	Gln	Leu	Pro	Lys	Trp	Pro	Tyr	Pro	Gln	
			520					525					530		•		
	gct	cct	tct	ggc	ccc	aca	ttc	tac	tcc	aaa	aca	ttt	cca	att	tta	ggc	1686
	Ala	Pro	Ser	Gly	Pro	Thr	Phe	Tyr	Ser	Lys	Thr	Phe	Pro	Ile	Leu	Gly	
		535					540					545					
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	Ser	Val	Gly	Asp	Thr	Phe	Leu	Tyr	Leu	Pro	Gly	Trp	Thr	Lys	Gly	Gln	•
	550					555					560				,	565	
	gtc	tgg	atc	aat	ggg	ttt	aac	ttg	ggc	cgg	tac	tgg	aca	aag	cag	ggg	1782
	Val	Trp	Ile	Asn	Gly	Phe	Asn	Leu	Gly	Arg	Tyr	Trp	Thr	Lys	Gln	Gly	
25					570					575					580		

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	Ser	Glu	Pro	Met	Glu	Leu	Ser	Gly	His									
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	tgga	accto	igg a	cato	gagt	g gg	gcago	gatco	ctt	ggto	jctg	gcca	acggt	ga (	ccta	aggaa	2384	
	ctaa	aggo	ca c	agto	ccto	et ga	atgt	aagt	aca	agta	ıcac	atto	ctto	jcc a	aaact	ttatt	2444	
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189/346

<211> 1450

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<213> Homo sapiens

5 <220>

<221> CDS

<222> (245)..(1417)

<400> 84

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Met Gly Met Asp Asp Cys Asp Ser Phe Phe Pro Gly Pro Leu Val

1 5 10 15

gct att att tgt gac ata ctt gga gag aaa act acc tcc att ctt ggg 337
Ala Ile Ile Cys Asp Ile Leu Gly Glu Lys Thr Thr Ser Ile Leu Gly

20 25 30

20 gct ttt gtt gtt act ggt gga tat ctg atc agc agc tgg gcc aca agt 385
Ala Phe Val Val Thr Gly Gly Tyr Leu Ile Ser Ser Trp Ala Thr Ser

35 40 45

att cct ttt ctt tgt gtg act atg gga ctt cta ccc ggt ttg ggt tct 433

Ile Pro Phe Leu Cys Val Thr Met Gly Leu Leu Pro Gly Leu Gly Ser

25 50 55 60

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	Ala	Phe	Leu	Tyr	Gln	Val	Ala	Ala	Val	Val	Thr	Thr	Lys	Tyr	Phe	Lys	
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	aaa	cga	ttg	gct	ctt	tct	aca	gct	att	gcc	cgt	tct	ggg	atg	gga	ctg	529
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	Pro	Ser	Ser	Met	Leu	Leu	Arg	Pro	Ile	His	Ile	Lys	Ser	Glu	Asn	Asn	
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25	gtc	tca	caa	aat	caa	agt	gaa	gag	ttc	tac	aat	ggg	cct	aac	agg	aac	865

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	aga	ctg	tta	tta	aag	agt	gat	gaa	gaa	agt	gat	aag	gtt	att	tcg	tgg	913
	Arg	Leu	Leu	Leu	Lys	Ser	Asp	Glu	Glu	Ser	Asp	Lys	Val	Ile	Ser	Trp	
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	Ser	Cys	Lys	Gln	Leu	Phe	Asp	Ile	Ser	Leu	Phe	Arg	Asn	Pro	Phe	Phe	
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	Met	Asp	Ala	Ser	Tyr	Leu	Val	Ser	Val	Ala	Gly	Ile	Leu	Glu	Thr	Val	
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	Ser	Gln	İle	Ile	Ser	Gly	Trp	Val	Ala	Asp	Gln	Asn	Trp	Ile	Lys	Lys	
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		305					310		•			315					
	ctt	gct	cct	tta	gcc	acc	aca	ttt	cca	cta	ctt	atg	acc	tac	acc	atc	1249
25	Leu	Ala	Pro	Leu	Ala	Thr	Thr	Phe	Pro	Leu	Leu	Met	Thr	Tyr	Thr	Ile	

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320 325 330 335 tgc ttt gcc atc ttt gct ggt ggt tac ctg gca ttg ata ctg cct gta 1297 Cys Phe Ala Ile Phe Ala Gly Gly Tyr Leu Ala Leu Ile Leu Pro Val 340 345 350 5 ctg gtt gat ctg tgt agg aat tct aca gta aac agg ttt ttg gga ctt 1345 Leu Val Asp Leu Cys Arg Asn Ser Thr Val Asn Arg Phe Leu Gly Leu 355 360 365 gcc agt ttc ttt gct ggg atg gct gtc ctt tct gga cca cct ata gca Ala Ser Phe Phe Ala Gly Met Ala Val Leu Ser Gly Pro Pro Ile Ala 10 370 375 380 ggt aac acc ttc acc aca ttc tga acaaatttca atagcaataa aagagaaaaa 1447 Gly Asn Thr Phe Thr Thr Phe 385 390 ctg 1450 15 <210> 85 <211> 1897 <212> DNA <213> Homo sapiens 20 <220> <221> CDS <222> (8)..(1366)

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	Lys	Asn	Phe	Ser	Glu	Leu	Pro	Leu	Val	Met	Trp	Leu	Gln	Gly	Gly	Pro	
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	gac	agt	gat	ctc	aaa	cca	cgg	aaa	acc	acc	tgg	ctc	cag	gct	gcc	agt	337
20			Asp										_	_		-	
	95					100		_			105					110	
	ctc	cta	ttt	gtg	gat	aat	ccc	ata	aac	act	aaa	ttc	agt	tat	ata		385
			Phe										-				
					115				1	120	1			-1-	125		
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	220	-90	990	900		900	uay	gac	cuy	guu	acy	grg	gul	Lua	gac	acy	433

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	175					180					185					190		
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	Asn	Ile	Leu	Thr	Lys	Ser	Thr	Pro	Thr	Ser	Thr	Met	Glu	Ser	Ser	Leu	
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197/346

<213> Homo sapiens

<220>

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Met Arg Pro Ala

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Phe Ala Leu Cys Leu Leu Trp Gln Ala Leu Trp Pro Gly Pro Gly Gly

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Gly Glu His Pro Thr Ala Asp Arg Ala Gly Cys Ser Ala Ser Gly Ala

tgc tac agc ctg cac cac gct acc atg aag cgg cag gcg gcc gag gag 198 Cys Tyr Ser Leu His His Ala Thr Met Lys Arg Gln Ala Ala Glu Glu

30

35

40 45 50

gcc tgc atc ctg cga ggt ggg gcg ctc agc acc gtg cgt gcg ggc gcc 246
Ala Cys Ile Leu Arg Gly Gly Ala Leu Ser Thr Val Arg Ala Gly Ala

55 60 65

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25 70 75 80

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	Glu	Pro	Gln	Arg	Ser	Cys	Thr	Ala	Arg	Arg	Cys	Ala	Val	Leu	Gln	Ala	
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20	tcc	aac	ttg	acc	aag	gag	ctc	aac	ttc	acc	acc	cgc	gcc	aag	gat	gcc	345
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25			100					105	-	-	-		110	-			

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	Ala	Glu	Cys	Ser	Arg	Gln	Thr	Gln	Leu	Ala	Leu	Glu	Glu	Lys	Ala	Val	
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35 40 45

Glu Thr Met Val Ile Gly Asn Tyr Arg Thr Gln Met Trp Asp Lys Gln

50 55 60

Lys Glu Val Phe Leu Pro Ser Thr Pro Gly Leu Gly Met His Val Glu

20 65 70 75 80

Val Lys Asp Pro Asp Gly Lys Val Val Leu Ser Arg Gln Tyr Gly Ser

85 90 95

Glu Gly Arg Phe Thr Phe Thr Ser His Thr Pro Gly Asp His Gln Ile

100 105 110

25 Cys Leu His Ser Asn Ser Thr Arg Met Ala Leu Phe Ala Gly Gly Lys

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Leu Arg Val His Leu Asp Ile Gln Val Gly Glu His Ala Asn Asn Tyr Pro Glu Ile Ala Ala Lys Asp Lys Leu Thr Glu Leu Gln Leu Arg Ala Arg Gln Leu Leu Asp Gln Val Glu Gln Ile Gln Lys Glu Gln Asp Tyr Gln Arg Tyr Arg Glu Glu Arg Phe Arg Leu Thr Ser Glu Ser Thr Asn Gln Arg Val Leu Trp Trp Ser Ile Ala Gln Thr Val Ile Leu Ile Leu Ģ Thr Gly Ile Trp Gln Met Arg His Leu Lys Ser Phe Phe Glu Ala Lys Lys Leu Val <210> 92 <211> 352 <212> PRT <213> Homo sapiens <400> 92 Met Glu Ser Gly Gly Arg Pro Ser Leu Cys Gln Phe Ile Leu Leu Gly Thr Thr Ser Val Val Thr Ala Ala Leu Tyr Ser Val Tyr Arg Gln Lys

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<212> PRT

<213> Homo sapiens

<400> 93

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		50					55					60				
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	65					70					75					80
10	Trp	Pro	Phe	Ala	Ala	Ile	Ser	Thr	Val	Cys	Cys	Pro	Glu	Lys	Leu	Thr
					85					90					95	
	His	Pro	Ile	Thr	Gly	Trp	Arg	Arg	Lys	Ile	Thr	Gln	Thr	Ala	Leu	Lys
				100					105					110		
	Phe	Leu	Gly	Arg	Ala	Met	Phe	Phe	Ser	Met	Gly	Phe	Ile	Val	Ala	Val
15			115					120					125			
	Lys	Gly	Lys	Ile	Ala	Ser	Pro	Leu	Glu	Ala	Pro	Val	Phe	Val	Ala	Ala
		130					135					140				
			Ser	Thr	Phe			Gly	Ile	Ala		Val	Val	Ala	Gly	
	145					150					155					160
20	Pro	Ser	Ile	Val			Asn	Glu	Asn			Val	Pro	Leu		GLY
				_	165			_		170					175	<b>D</b>
	Arg	Leu	Leu	_		Val	. Gin	Pro			. Val	Ser	Arg			Pro
	_	_		180		mt.	. Tl-	. 3	185		<b>-</b> 1 -	•	<b>n</b>	190		50-
25	Asp	ser	Arg		Asn	TOX	тте	200		i iie	тте	. Lys	arg 205		TIIT	sei

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Gly Gly Glu Trp Pro Gln Ile Leu Val Phe Pro Glu Gly Thr Cys Thr Asn Arg Ser Cys Leu Ile Thr Phe Lys Pro Gly Ala Phe Ile Pro Gly Val Pro Val Gln Pro Val Leu Leu Arg Tyr Pro Asn Lys Leu Asp Thr Val Thr Trp Thr Trp Gln Gly Tyr Thr Phe Ile Gln Leu Cys Met Leu Thr Phe Cys Gln Leu Phe Thr Lys Val Glu Val Glu Met Phe Leu Phe Phe Trp Glu Gly Ser Ser Lys His Cys Leu Lys Ile Ser Ser Phe Phe Cys Ile Phe Ser Leu Arg Arg Phe Lys Arg Arg Ile Thr Gln Arg Thr Arg Thr Ala His Leu Leu Arg Leu Ser Phe <210> 95 <211> 350 <212> PRT <213> Homo sapiens <400> 95 Met Ala Leu Pro Pro Gly Pro Ala Ala Leu Arg His Thr Leu Leu Leu

. 5

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Ala Cys Leu Val Cys Arg Lys Glu Lys Lys Thr Lys Gly Pro Ser Arg His Pro Ser Leu Ile Ser Ser Asp Ser Asn Asn Leu Lys Leu Asn Asn Val Arg Leu Pro Arg Glu Asn Met Ser Leu Pro Ser Asn Leu Gln Leu Asn Asp Leu Thr Pro Asp Ser Arg Ala Val Lys Pro Ala Asp Arg Gln Met Ala Gln Asn Asn Ser Arg Pro Glu Leu Leu Asp Pro Glu Pro Gly Gly Leu Leu Thr Ser Gln Ala Cys Leu Leu His His Gly Thr Pro Ala Leu Thr Asn Pro Trp Leu Pro His Gln Glu Gly Ala Leu Pro Gly Gly Trp Ser Pro Gln Ala His Asn Ser Thr Val Trp Lys Leu 

<210> 96

20 <211> 113

<212> PRT

<213> Homo sapiens

<400> 96

25 Met Asn Glu Thr Asn Lys Thr Leu Val Gly Pro Ser Glu Leu Pro Thr

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Ala Ser Ala Val Ala Pro Gly Pro Gly Thr Gly Ala Arg Ala Trp Pro Val Leu Val Gly Phe Val Leu Gly Ala Val Val Leu Ser Leu Leu Ile Ala Leu Ala Ala Lys Cys His Leu Cys Arg Arg Tyr His Ala Ser Tyr Arg His Arg Pro Leu Pro Glu Thr Gly Arg Gly Gly Arg Pro Gln Val Ala Glu Asp Glu Asp Asp Asp Gly Phe Ile Glu Asp Asn Tyr Ile Gln Pro Gly Thr Gly Glu Leu Gly Thr Glu Gly Ser Arg Asp His Phe Ser Leu <210> 97 <211> 189 <212> PRT <213> Homo sapiens <400> 97 Met Ala Leu Leu Ser Arg Pro Ala Leu Thr Leu Leu Leu Leu Met 

Ala Ala Val Val Arg Cys Gln Glu Gln Ala Gln Thr Thr Asp Trp Arg

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				20					25					30		
	Ala	Thr	Leu	Lys	Thr	Ile	Arg	Asn	Gly	Val	His	Lys	Ile	Asp	Thr	Tyr
			35					40					45			
	Leu	Asn	Ala	Ala	Leu	Asp	Leu	Leu	Gly	Gly	Glu	Asp	Gly	Leu	Cys	Gln
5		50					55					60				
	Tyr	Lys	Cys	Ser	Asp	Gly	Ser	Lys	Pro	Phe	Pro	Arg	Tyr	Gly	Tyr	Lys
	65					70					<b>7</b> 5					80
	Pro	Ser	Pro	Pro	Asn	Gly	Cys	Gly	Ser	Pro	Leu	Phe	Gly	Val	His	Leu
					85					90					95	
10	Asn	Ile	Gly	Ile	Pro	Ser	Leu	Thr	Lys	Cys	Cys	Asn	Gln	His	Asp	Arg
				100					105					110		
	Суѕ	Tyr	Glu	Thr	Cys	Gly	Lys	Ser	Lys	Asn	Asp	Cys	Asp	Glu	Glu	Phe
			115					120					125			
	Gln	Tyr	Cys	Leu	Ser	Lys	Ile	Cys	Arg	Asp	Val	Gln	Lys	Thr	Leu	Gly
15		130					135					140				
	Leu	Thr	Gln	His	Val	Gln	Ala	Cys	Glu	Thr	Thr	Val	Glu	Leu	Leu	Phe
	145					150					155					160
	Asp	Ser	Val	Ile	His	Leu	Gly	Cys	Lys	Pro	Tyr	Leu	Asp	Ser	Gln	Arg
					165					170					175	
20	Ala	Ala	Cys	Arg	Cys	His	Tyr	Glu	Glu	Lys	Thr	Asp	Leu			
				180					185							
		)> 98														
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25

<212> PRT

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<213> Homo sapiens

_	-	_	
<4	n	n 🔪	98

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5	1				5					10					15	
	Ser	Leu	Gly	Leu	Met	Leu	Ser	Val	Val	Leu	Leu	Met	Gly	Leu	Ala	Arg
				20					25					30		
	Val	Val	Ala	Arg	Gln	Gln	Leu	His	Arg	Pro	Val	Ala	His	Ala	Phe	Val
			35					40		•			45			
10	Leu	Glu	Phe	Leu	Ala	Thr	Phe	Gln	Leu	Cys	Суѕ	Суѕ	Thr	His	Glu	Leu
		50					55					60				
	Gln	Leu	Leu	Ser	Glu	Gln	His	Pro	Ala	His	Pro	Thr	Trp	Thr	Leu	Thr
	65					70					75					80
	Leu	Val	Tyr	Phe	Phe	Ser	Leu	Val	His	Gly	Leu	Thr	Leu	Val	Gly	Thr
15					85					90					95	
	Ser	Ser	Asn	Pro	Cys	Gly	Val	Met	Met	<b>Gl</b> n	Met	Met	Leu	Gly	Gly	Met
				100					105					110		
	Ser	Pro	Glu	Thr	Gly	Ala	Val	Arg	Leu	Leu	Ala	Gln	Leu	Val	Ser	Ala
		٠	115					120					125			
20	Leu	Cys	Ser	Arg	Tyr	Cys	Thr	Ser	Ala	Leu	Trp	Ser	Leu	Gly	Leu	Thr
		130					135					140				
	Gln	Tyr	His	Val	Ser	Glu	Arg	Ser	Phe	Ala	Cys	Lys	Asn	Pro	Ile	Arg
	145					150					155					160
	Val	Asp	Leu	Leu	Lys	Ala	Val	Ile	Thr	Glu	Ala	Val	Cys	Ser	Phe	Leu
25					165					170					175	

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	Phe	His	Ser	Ala	Leu	Leu	His	Phe	Gln	Glu	Val	Arg	Thr	Lys	Leu	Arg
				180					185					190		
	Ile	His	Leu	Leu	Ala	Ala	Leu	Ile	Thr	Phe	Leu	Val	Tyr	Ala	Gly	Gly
			195					200					205			
5	Ser	Leu	Thr	Gly	Ala	Val	Phe	Asn	Pro	Ala	Leu	Ala	Leu	Ser	Leu	His
		210					215					220				
	Phe	Met	Cys	Phe	Asp	Glu	Ala	Phe	Pro	Gln	Phe	Phe	Ile	Val	Tyr	Trp
	225					230					235					240
	Leu	Ala	Pro	Ser	Leu	Gly	Ile	Leu	Leu	Met	Ile	Leu	Met	Phe	Ser	Phe
10					245					250					255	
	Phe	His	Gly	Cys	Ile	Thr	Thr	Ile	Gln	Leu	Ile	Lys	Arg	Asn	Asn	Cys
				260					265					270		
	Ser	Lys	Asp	Ser	Asp		•									
			275													
15						•										
	<210	)> 99														
	<211	.> 27	74													
	<212	!> PF	₹T													
	<213	3> Hc	omo s	sapie	ens											
20																
	<400	)> 99	)													
	Met	Gly	Lys	Ser	Leu	Ser	His	Leu	Pro	Leu	His	Ser	Ser	Lys	Glu	Asp
•	1				5					10					15	
	Ala	Tyr	Asp	Gly	Val	Thr	Ser	Glu	Asn	Met	Arg	Asn	Gly	Leu	Val	Asn
25				20					25					30		

	Ser	Glu	Val	His	Àsn	Glu	Asp	Gly	Arg	Asn	Gly	Asp	Val	Ser	Gln	Phe
			35					40					45			
	Pro	Tyr	Val	Glu	Phe	Thr	Gly	Arg	Asp	Ser	Val	Thr	Cys	Pro	Thr	Cys
	'	50					55			-		60				
5	Gln	Gly	Thr	Gly	Arg	Ile	Pro	Arg	Gly	Gln	Glu	Asn	Gln	Leu	Val	Ala
	65					70					75					80
	Leu	Ile	Pro	Tyr	Ser	Asp	Gln	Arg	Leu	Arg	Pro	Arg	Arg	Thr	Lys	Leu
	-				85					90					95	
	Tyr	Val	Met	Ala	Ser	Val	Phe	Val	Cys	Leu	Leu	Leu	Ser	Gly	Leu	Ala
10				100					105					110		
	Val	Phe	Phe	Leu	Phe	Pro	Arg	Ser	Ile	Asp	Val	Lys	Tyr	Ile	Gly	Val
			115					120					125			
	Lys	Ser	Ala	Tyr	Val	Ser	Tyr	Asp	Val	Gln	Lys	Arg	Thr	Ile	Tyr	Leu
		130					135					140				
15	Asn	Ile	Thr	Asn	Thr	Leu	Asn	Ile	Thr	Asn	Asn	Asn	Tyr	Tyr	Ser	Val
	145					150					155					160
	Glu	Val	Glu	Asn	Ile	Thr	Ala	Gln	Val	Gln	Phe	Ser	Lys	Thr	Val	Ile
					165					170					175	
	Gly	Lys	Ala	Arg	Leu	Asn	Asn	Ile	Thr	Ile	Ile	Gly	Pro	Leu	Asp	Met
20				180					185					190		
	Lys	Gln	Ile	Asp	Tyr	Thr	Val	Pro	Thr	Val	Ile	Ala	Glu	Glu	Met	Ser
			195					200					205			
	Tyr	Met	Tyr	Asp	Phe	Cys	Thr	Leu	Ile	Ser	Ile	Lys	Val	His	Asn	Ile
		210					215					220				
25	Val	Leu	Met	Met	Gln	Val	Thr	Val	Thr	Thr	Thr	Tvr	Phe	Gly	His	Ser

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Glu Gln Ile Ser Gln Glu Arg Tyr Gln Tyr Val Asp Cys Gly Arg Asn Thr Thr Tyr Gln Leu Gly Gln Ser Glu Tyr Leu Asn Val Leu Gln Pro Gln Gln <210> 100 <211> 390 <212> PRT <213> Homo sapiens <400> 100 Met Ile Ser Leu Pro Gly Pro Leu Val Thr Asn Leu Leu Arg Phe Leu Phe Leu Gly Leu Ser Ala Leu Ala Pro Pro Ser Arg Ala Gln Leu Gln Leu His Leu Pro Ala Asn Arg Leu Gln Ala Val Glu Gly Gly Glu Val Val Leu Pro Ala Trp Tyr Thr Leu His Gly Glu Val Ser Ser Ser Gln Pro Trp Glu Val Pro Phe Val Met Trp Phe Phe Lys Gln Lys Glu Lys Glu Asp Gln Val Leu Ser Tyr Ile Asn Gly Val Thr Thr Ser Lys Pro

					85					90					95	
	Gly	Val	Ser	Leu	Val	Tyr	Ser	Met	Pro	Ser	Arg	Asn	Leu	Ser	Leu	Arg
				100					105					110		
	Leu	Glu	Gly	Leu	Gln	Glu	Lys	Asp	Ser	Gly	Pro	Tyr	Ser	Cys	Ser	Val
5			115					120					125			
	Asn	Val	Gln	Asp	Lys	Gln	Gly	Lys	Ser	Arg	Gly	His	Ser	Ile	Lys	Thr
		130					135					140				
	Leu	Glu	Leu	Asn	Val	Leu	Val	Pro	Pro	Ala	Pro	Pro	Ser	Cys	Arg	Leu
	145					150					155					160
LO	Gln	Gly	Val	Pro	His	Val	Gly	Ala	Asn	Val	Thr	Leu	Ser	Cys	Gln	Ser
					165					170					175	
	Pro	Arg	Ser	Lys	Pro	Ala	۷al	Gln	Tyr	Gln	Trp	Asp	Arg	Gln	Leu	Pro
				180					185					190		
	Ser	Phe	Gln	Thr	Phe	Phe	Ala	Pro	Ala	Leu	Asp	Val	Ile	Arg	Gly	Ser
L5			195					200					205			
	Leu	Ser	Leu	Thr	Asn	Leu	Ser	Ser	Ser	Met	Ala	Gly	Val	Tyr	Val	Cys
		210					215					220				
	Lys	Ala	His	Asn	Glu	Val	Gly	Thr	Ala.	Gln	Cys	Asn	Val	Thr	Leu	Glu
	225					230					235					240
20	Val	Ser	Thr	Gly	Pro	Gly	Ala	Ala	Val	Val	Ala	Gly	Ala	Val	Val	Gly
					245					250					255	
	Thr	Leu	Val	Gly	Leu	Gly	Leu	Leu	Ala	Gly	Leu	Val	Leu	Leu	Tyr	His
				260					265					270		
	Cys	Arg	Gly	Lys	Ala	Leu	Glu	Glu	Pro	Ala	Asn	Asp	Ile	Lys	Glu	Asp
25			275					280					285			

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Ala Ile Ala Pro Arg Thr Leu Pro Trp Pro Lys Ser Ser Asp Thr Ile 290 295 300 Ser Lys Asn Gly Thr Leu Ser Ser Val Thr Ser Ala Arg Ala Leu Arg 305 310 315 320 5 Pro Pro His Gly Pro Pro Arg Pro Gly Ala Leu Thr Pro Thr Pro Ser 325 330 335 Leu Ser Ser Gln Ala Leu Pro Ser Pro Arg Leu Pro Thr Thr Asp Gly 340 345 350 Ala His Pro Gln Pro Ile Ser Pro Ile Pro Gly Gly Val Ser Ser Ser 10 355 360 365 Gly Leu Ser Arg Met Gly Ala Val Pro Val Met Val Pro Ala Gln Ser 370 375 380 Gln Ala Gly Ser Leu Val 385 390 15 <210> 101 <211> 684 <212> DNA <213> Homo sapiens 20 <400> 101 atggcaggtg tcggggctgg gcctctgcgg gcgatggggc ggcaggccct gctgcttctc 60 gcgctgtgcg ccacaggcgc ccaggggctc tacttccaca tcggcgagac cgagaagcgc 120 tgtttcatcg aggaaatccc cgacgagacc atggtcatcg gcaactatcg tacccagatg 180 25 tgggataagc agaaggaggt cttcctgccc tcgacccctg gcctgggcat gcacgtggaa 240

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gtgaaggacc ccgacggcaa ggtggtgctg tcccggcagt acggctcgga gggccgcttc 300
acgttcacct cccacacgcc cggtgaccat caaatctgtc tgcactccaa ttctaccagg 360
atggctctct tcgctggtgg caaactgcgg gtgcatctcg acatccaggt tggggagcat 420
gccaacaact accctgagat tgctgcaaaa gataagctga cggagctaca gctccgcgcc 480
cgccagttgc ttgatcaggt ggaacagatt cagaaggagc acgattacca aaggtatcgt 540
gaagagcgct tccgactgac gagcgagagc accaaccaga gggtcctatg gtggtccatt 600
gctcagactg tcatcctcat cctcactggc atctggcaga tgcgtcacct caagagcttc 660
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10 <210> 102

5

<211> 1059

<212> DNA

<213> Homo sapiens

15 <400> 102

20

25

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ctggtcctgg acaacaacte tgtccgcctg cagccgcca aacaaggcat gcagtactat 660 ctaagcagcc aggacttcga cagcctgctg cagaggcagg agtcgagcgt caggctctgg 720 aaggtgctgg cgctggtttt tggctttgcc acatgtgcca ccctcttctt cattctccgg 780 aagcagtate tgcagcggca ggagcgcctg cgcctcaagc agatgcagga ggagttccag 840 gagcatgagg cccagctgct gagccgagcc aagcctgagg acagggagag tctgaagagc 900 gcctgtgtag tgtgtctgag cagcttcaag tcctgcgtct ttctggagtg tgggcacgtt 960 tgttcctgca ccgagtgcta ccgcgccttg ccagagccca agaagtgccc tatctgcaga 1020 caggcgatca cccgggtgat acccctgtac aacagctaa

10 <210> 103

5

<211> 393

<212> DNA

<213> Homo sapiens

15 <400> 103

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<210> 104

25 <211> 993

20

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<212> DNA

<213> Homo sapiens

<400> 104

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<210> 105

<211> 1053

25 <212> DNA

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#### <213> Homo sapiens

<400> 105

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<210> 106

<211> 342

25 <212> DNA

WO 01/49728

### 238/346

PCT/JP00/09359

<213> Homo sapiens

<400> 106

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10

5

<210> 107

<211> 570

<212> DNA

<213> Homo sapiens

15

20

25

<400> 107

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ggegtteata agatagaeae gtaeetgaae geegeettgg aceteetggg aggegaggae 180
ggtetetgee agtataaatg eagtgaegga tetaageett teecaegtta tggttataaa 240
eeeteeceae egaatggatg tggeteteea etgtttggtg tteatettaa eattggtate 300
eetteeetga eaaagtgttg eaaceaaeae gaeaggtget atgaaaeetg tggeaaaage 360
aagaatgaet gtgatgaaga atteeagtat tgeeteteea agatetgeeg agatgtaeag 420
aaaacaetag gaetaaetea geatgtteag geatgtgaaa eaacagtgga getettgttt 480
gaeagtgtta taeatttagg ttgtaaaeea tatetggaea geeaaegage egeatgeagg 540

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tgtcattatg aagaaaaac tgatctttaa 570

<210> 108

<211> 834

5 <212> DNA

10

15

20

<213> Homo sapiens

<400> 108

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aggeeggtgg eecacgeett egteetggag tttetageea eetteeaget etgetgetge 180
acceaegage tgeaactget gagegaacag eaceeegge acceeacetg gaegetgaeg 240
etegtetaet tetteteget tgtgeatgge etgaetetgg tgggeaegte eageaaceeg 300
tgeggegtga tgatgeagat gatgetgggg ggeatgteee eegagaeggg tgeggtgagg 360
etattggete agetggttag tgeeetgtge ageaggtaet geacaagege ettgtggage 420
ttgggtetga eccagtatea egteagegag aggagetteg ettgeaagaa teecateega 480
gtegaettge teaaageggt eateacagag geegtetget eettetett eeacageget 540
etgetgeaet teeaggaagt eegaaceaag ettegtatee acetgetgge tgeaeteate 600
acetttttgg tetatgeagg aggaagteta acaggagetg tatttaatee agetttggea 660
etttegetae attteatgtg ttttgatgaa geatteeete agttttttat agtataetgg 720
etggeteett etttaggtat attgttgatg attttgatgt teagetttt ceatggetge 780
ataacaacea tacaattaat aaaaaggaat aactgtteea aagaeteaga etaa 834

<210> 109

25 <211> 825

### 240/346

<212> DNA

<213> Homo sapiens

<400> 109

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20 <210> 110

<211> 1173

<212> DNA

<213> Homo sapiens

25 <400> 110

## 241/346

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<210> 111

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15

20

<211> 1894

<212> DNA

25 <213> Homo sapiens

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								1				5		
10	ggg cct d	ctg cgg	gcg a	tg ggg	cgg	cag	gcc	ctg	ctg	ctt	ctc	gcg	ctg	101
	Gly Pro I	Leu Arg	Ala M	et Gly	Arg	Gln	Ala	Leu	Leu	Leu	Leu	Ala	Leu	
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	tgc gcc a	aca ggc	gcc c	ag ggg	ctc	tac	ttc	cac	atc	ggc	gag	acc	gag	149
	Cys Ala I	hr Gly	Ala G	ln Gly	Leu	Tyr	Phe	His	Ile	Gly	Glu	Thr	Glu	
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	aag cgc t	gt ttc	atc g	ag gaa	atc	ccc	gac	gag	acc	atg	gtc	atc	ggc	197
	Lys Arg C	Cys Phe	Ile G	lu Glu	Ile	Pro	Asp	Glu	Thr	Met	Val	Ile	Gly	
	40			45					50					
	aac tat c	gt acc	cag a	tg tgg	gat	aag	cag	aag	gag	gtc	ttc	ctg	ccc	245
20	Asn Tyr A	rg Thr	Gln M	et Trp	Asp	Lys	Gln	Lys	Glu	Val	Phe	Leu	Pro	
	55			60				65					70	
	tcg acc c	ct ggc	ctg g	gc atg	cac	gtg	gaa	gtg	aag	gac	ccc	gac	ggc	293
	Ser Thr P	ro Gly	Leu G	ly Met	His	Val	Glu	Val	Lys	Asp	Pro	Asp	Gly	
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		Lys	Val	Val	Leu	Ser	Arg	Gln	Tyr	Gly	Ser	Glu	Gly	Arg	Phe	Thr	Phe	
					90					95					100			
		acc	tcc	cac	acg	ccc	ggt	gac	cat	caa	atc	tgt	ctg	cac	tcc	aat	tct	389
		Thr	Ser	His	Thr	Pro	Gly	Asp	His	Gln	Ile	Cys	Leu	His	Ser	Asn	Ser	
	5			105					110					115				
		acc	agg	atg	gct	ctc	ttc	gct	ggt	ggc	aaa	ctg	cgg	gtg	cat	ctc	gac	437
		Thr	Arg	Met	Ala	Leu	Phe	Ala	Gly	Gly	Lys	Leu	Arg	Val	His	Leu	Asp	
			120					125					130					
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1	0	Ile	Gln	Val	Gly	Glu	His	Ala	Asn	Asn	Tyr	Pro	Glu	Ile	Ala	Ala	Lys	
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		gat	aag	ctg	acg	gag	cta	cag	ctc	cgc	gcc	cgc	cag	ttg	ctt	gat	cag	533
		Asp	Lys	Leu	Thr	Glu	Leu	Gln	Leu	Arg	Ala	Arg	Gln	Leu	Leu	Asp	Gln	
						15 <b>5</b>					160					165		
1	5	gtg	gaa	cag	att	cag	aag	gag	cag	gat	tac	caa	agg	tat	cgt	gaa	gag	581
		Val	Glu	Gln	Ile	Gln	Lys	Glu	Gln	Asp	Tyr	Gln	Arg	Tyr	Arg	Glu	Glu	
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		cgc	ttc	cga	ctg	acg	agc	gag	agc	acc	aac	cag	agg	gtc	cta	tgg	tgg	629
		Arg	Phe	Arg	Leu	Thr	Ser	Glu	Ser	Thr	Asn	Gln	Arg	Val	Leu	Trp	Trp	
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		tcc	att	gct	cag	act	gtc	atc	ctc	atc	ctc	act	ggc	atc	tgg	cag	atg	677
		Ser	Ile	Ala	Gln	Thr	Val	Ile	Leu	Ile	Leu	Thr	Gly	Ile	Trp	Gln	Met	
			200					205					210					
		cgt	cac	ctc	aag	agc	ttc	ttt	gag	gcc	aag	aag	ctg	gtg	tag			719
2	5	Arg	His	Leu	Lys	Ser	Phe	Phe	Glu	Ala	Lys	Lys	Leu	Val				

#### 244/346

215 220 225

tgccctcttt gtatgaccct tcctttttac ctcatttatt tggtactttc cccacacagt 779 cctttatcca cctggatttt tagggaaaaa aatgaaaaag aataagtcac attggttcca 839 tggccacaaa ccattcagat cagccacttg ctgaccctgg ttcttaagga cacatgacat 899 tagtccaatc tttcaaaatc ttgtcttagg gcttgtgagg aatcagaact aacccaggac 959 tcaqtcctqc ttcttttqcc tcqaqtqatt ttcctctqtt tttcactaaa taaqcaaatq 1019 aaaactctct ccattacctt ctgctttctc tttgtccact tacgcagtag gtgactggca 1079 tgtgccacag agcaggccct gcctcactgt ctgctggtca gttctgggtt cacttaatgg 1139 📑 ctttgtgaat gtaaataagg ggcaggtctt ggccctagag gattgagatg tttttctaaa 1199 tottagaact attittggat aaattatata tittoottoo tagtagaagt gitactgoot 1259 gtaactaget caaaatacca atgcagttte tgcattetgg gttttgtttt teettttttt 1319 tttttttttt ttttttgag ttttgctctt gtcgcccagg ctggagtgca atggcgtgat 1379 ctcagctcac tggcaacatc tgcctcccgg gttcaaatga ttctcctgcc tcagtctcct 1439 gagtagctgg gattacaggt gcccgccacc acgctcagct aatttttgta tttttagtag 1499 agatggggtt ttaccatgtt ggccaggctg gtcttagact cctgacctca gttgatccac 1559 ctgcctcagc ctctgcattc agtttattca catatttttg gtaactccca tggcaqctcc 1619 taggatttca gcggtctgtg ggccagaaag caggcaccag ggctgacctc aaggccgtat 1679 cagagggcca agcagagttc ttttggatac ctgcttttca tcccacaggg ccttagagtc 1739 agaggtaagg tagcaacaga gctagaatgg ggcaatgcac tcttaccctc cttctcaact 1799 tttatttaag ctgtgctaaa tgttttcttc aagggaacca gatttagttc tttacagaat 1859 tttccagtga aataaactct catgttattg ttccc 1894

<210> 112

<211> 2413

25 <212> DNA

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15

20

### 245/346

<213> Homo sapiens

<220>

<221> CDS

5 <222> (115)..(1173)

<400> 112

15

25

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. 10 Met

1

gag agc gga ggg cgg ccc tcg ctg tgc cag ttc atc ctc ctg ggc acc 165 Glu Ser Gly Gly Arg Pro Ser Leu Cys Gln Phe Ile Leu Leu Gly Thr

5 10 15

acc tct gtg gtc acc gcc gcc ctg tac tcc gtg tac cgg cag aag gcc 213

Thr Ser Val Val Thr Ala Ala Leu Tyr Ser Val Tyr Arg Gln Lys Ala

20 25 30

cgg gtc tcc caa gag ctc aag gga gct aaa aaa gtt cat ttg ggt gaa 261
Arg Val Ser Gln Glu Leu Lys Gly Ala Lys Lys Val His Leu Gly Glu

20 35 40 45

gat tta aag agt att ctt tca gaa gct cca gga aaa tgc gtg cct tat 309

Asp Leu Lys Ser Ile Leu Ser Glu Ala Pro Gly Lys Cys Val Pro Tyr

50 55 60 65

gct gtt ata gaa gga gct gtg cgg tct gtt aaa gaa acg ctt aac agc 357
Ala Val Ile Glu Gly Ala Val Arg Ser Val Lys Glu Thr Leu Asn Ser

					70					75					80		
	cag	ttt	gtg	gaa	aac	tgc	aag	ggg	gta	att	cag	cgg	ctg	aca	ctt	cag	405
	Gln	Phe	Val	Glu	Asn	Cys	Lys	Gly	Val	Ile	Gln	Arg	Leu	Thr	Leu	Gln	
				85					90					95			
5	gag	cac	aag	atg	gtg	tgg	aat	cga	acc	acc	cac	ctt	tgg	aat	gat	tgc	453
	Glu	His	Lys	Met	Val	Trp	Asn	Arg	Thr	Thr	His	Leu	Trp	Asn	Asp	Cys	٠
			100					105					110				
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	Ser	Lys	Ile	Ile	His	Gln	Arg	Thr	Asn	Thr	Val	Pro	Phe	Asp	Leu	Val	
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	Pro	His	Glu	Asp	Gly	Val	Asp	Val	Ala	Val	Arg	Val	Leu	Lys	Pro	Leu	
	130					135					140					145	
	gac	tca	gtg	gat	ctg	ggt	cta	gag	act	gtg	tat	gag	aag	ttc	cac	ccc	597
15	Asp	Ser	Val	Asp	Leu	Gly	Leu	Glu	Thr	Val	Tyr	Glu	Lys	Phe	His	Pro	
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	tcg	att	cag	tcc	ttc	acc	gat	gtc	atc	ggc	cac	tac	atc	agc	ggt	gag	645
	Ser	Ile	Gln	Ser	Phe	Thr	Asp	Val	Ile	Gly	His	Tyr	Ile	Ser	Gly	Glu	
				165					170					175			
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	Arg	Pro	Lys	Gly	Ile	Gln	Glu	Thr	Glu	Glu	Met	Leu	Lys	Val	Gly	Ala	
			180					185					190			•	
	acc	ctc	aca	ggg	gtt	ggc	gaa	ctg	gtc	ctg	gac	aac	aac	tct	gtc	cgc	741
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# 247/346

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	Leu	Gln	Pro	Pro	Lys	Gln	Gly	Met	Gln	Tyr	Tyr	Leu	Ser	Ser	Gln	Asp	
	210					215					220					225	
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5	Phe	Asp	Ser	Leu	Leu	Gln	Arg	Gln	Glu	Ser	Ser	Val	Arg	Leu	Trp	Lys	
					230					235					240		
	gtg	ctg	gcg	ctg	gtt	ttt	ggc	ttt	gcc	aca	tgt	gcc	acc	ctc	ttc	ttc	885
	Val	Leu	Ala	Leu	Val	Phe	Gly	Phe	Ala	Thr	Cys	Ala	Thr	Leu	Phe	Phe	
				245					250					255			
10	att	ctc	cgg	aag	cag	tat	ctg	cag	cgg	cag	gag	cgc	ctg	cgc	ctc	aag	933
	Ile	Leu	Arg	Lys	Gln	Tyr	Leu	Gln	Arg	Gln	Glu	Arg	Leu	Arg	Leu	Lys	
			260					265					270				
	cag	atg	cag	gag	gag	ttc	cag	gag	cat	gag	gcc	cag	ctg	ctg	agc	cga	981
	Gln	Met	Gln	Glu	Glu	Phe	Gln	Glu	His	Glu	Ala	Gln	Leu	Leu	Ser	Arg	
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	gcc	aag	cct	gag	gac	agg	gag	agt	ctg	aag	agc	gcc	tgt	gta	gtg	tgt	1029
	Ala	Lys	Pro	Glu	Asp	Arg	Glu	Ser	Leu	Lys	Ser	Ala	Cys	Val	Val	Cys	
	290					295					300					305	
	ctg	agc	agc	ttc	aag	tcc	tgc	gtc	ttt	ctg	gag	tgt	ggg	cac	gtt	tgt	1077
20	Leu	Ser	Ser	Phe	Lys	Ser	Cys	Val	Phe	Leu	Glu	Cys	Gly	His	Val	Cys	
					310					315					320		
	tcc	tgc	acc	gag	tgc	tac	cgc	gcc	ttg	cca	gag	ccc	aag	aag	tgc	cct	1125
	Ser	Cys	Thr	Glu	Cys	Tyr	Arg	Ala	Leu	Pro	Glu	Pro	Lys	Lys	Cys	Pro	
				325					330					335			
25	atc	tgc	aga	cag	gcg	atc	acc	cgg	gtg	ata	ccc	ctg	tac	aac	agc	taa	1173

9

#### 248/346

Ile Cys Arg Gln Ala Ile Thr Arg Val Ile Pro Leu Tyr Asn Ser

340 345 350

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25 <210> 113

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15

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249/346

<211> 2376

<212> DNA

<213> Homo sapiens

5 <220>

<221> CDS

<222> (35)..(427)

<400> 113

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ccc ggg gcg tcc gcc agc tct gcg ccg ccc gcg cag gaa gag ggc atg 103
Pro Gly Ala Ser Ala Ser Ser Ala Pro Pro Ala Gln Glu Glu Gly Met

15 10 15 20

60

acg tgg tgg tac cgc tgg ctg tgt cgc ctg tct ggg gtg ctg ggg gca 151
Thr Trp Trp Tyr Arg Trp Leu Cys Arg Leu Ser Gly Val Leu Gly Ala

25 30 35

gtc tct tgc gcg atc tct ggc ctc ttc aac tgc atc acc atc cac cct 199

Val Ser Cys Ala Ile Ser Gly Leu Phe Asn Cys Ile Thr Ile His Pro

40 45 50 55

ctg aac atc gcg gcc ggc gtg tgg atg atg atg gcg gtc gtt ccc atc 247
Leu Asn Ile Ala Ala Gly Val Trp Met Met Ala Val Val Pro Ile

65 70

gtc atc agc ctg acc ctg acc acg ctg ctg ggc aac gcc atc gcc ttt 295

	Val Ile Se	r Leu Thr I	eu Thr Thr	Leu Leu Gly	Asn Ala Ile Ala Phe	
		75		80	85	
	gct acg gg	g gtg ctg t	ac gga ctc	tct gct ctg	ggc aaa aag ggc gat	343
	Ala Thr Gl	y Val Leu I	yr Gly Leu	Ser Ala Leu	Gly Lys Lys Gly Asp	
5	9	0	95		100	
	gcg atc tc	c tat gcc a	agg atc cag	cag cag agg	cag cag gcg gat gag	391
	Ala Ile Se	r Tyr Ala A	rg Ile Gln	Gln Gln Arg	Gln Gln Ala Asp Glu	
	105		110		115	
	gag aag ct	c gcg gag a	acc ctg gag	ggg gag ctg	tga agggctgggc	437
10	Glu Lys Le	u Ala Glu T	hr Leu Glu	Gly Glu Leu		
	120	1	.25	130		
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	ccacgctgag	gcacagcctg	g gagaggggcc	tttgcacgtg	tccctacacc tggagtcctc	557
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	gggcctggga	cagcctgccg	g ctgccagcaa	cctcccactg	ctgcctaggg tgcagcgccc	917
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	aactgcagcc	ttggcagtga	a ctggacagct	gggtggggga	tgeteeetge tggeeetggg	1037
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	cccctaggtt	ctgcccatca	a ccccccgccc	: ctgctggcct	gcccaagccc tgccctcagg	1157
	gagettetge	cttttaagaa	a ctgggcagag	gccacagtca	cctccccaca cagagetgte	1217
25	cccactgccc	tgggtgccag	g gctgtccgga	gccaggccta	cccagggagg atgcagagag	1277

## 251/346

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	cccaggtggg	gcttggcaga	agcgggcggg	tgtggaagat	attccatctg	gggccaaccc	1457
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	ggagtctggc	cagctgagcc	ccagggtggc	aggggcatta	tagcctggtg	gacatgtgcc	1757
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	cctacccagg	tagtgggacc	ccgggccccc	ttctgcctgg	cttgcctgct	tctgcccttt	1997
	ccagaggggt	ctcactgaca	gccagagaca	gcaggagaag	ggttggctgt	ggatcaagga	2057
	aggctgcccc	tgtaccctgt	ggggaaatgg	tgggtgcatg	gctggatgca	gaggtggaag	2117
15	gccctgggcc	acaggcgaga	gtgggcgtgt	cacctgtccc	aggttcccag	caagtctgca	2177
	gctgtgcagt	cctggggtcc	ctgaccctgt	cgcccagggg	gcgtgctgtc	cagcaggggc	2237
	cctgccttgc	aaggaacgtc	tcttccggcg	gctgggccgc	tcctgcctgg	tctgggctgt	2297
	gtgtggcgcc	ctttcctcct	tgtttgttcc	tctgtgttct	gtgtgcgtct	taagcaataa	2357
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<210> 114

<211> 1155

<212> DNA

<213> Homo sapiens

252/346

<220>

<221> CDS

<222> (110)..(1102)

5

20

5 <400> 114

gaggeteece agegtegeee taggetggga etetagtagg tetteggete agttttgget 60 geagegeeeg egtagatege tteggeeggg ttetaegeee ggeteaact atg age egg 118 Met Ser Arg

1

10 tgc gcc cag gcg gcg gaa gtg gcg gcc aca gtg cca ggt gcc ggc gtc 166
Cys Ala Gln Ala Ala Glu Val Ala Ala Thr Val Pro Gly Ala Gly Val

10 15

ggg aac gtg ggg ctg cgg ccc ccc atg gtg ccc cgt cag gcg tcc ttc 214
Gly Asn Val Gly Leu Arg Pro Pro Met Val Pro Arg Gln Ala Ser Phe

15 20 25 30 35

ttc ccg ccg ccg gtg ccg aac ccc ttc gtg cag cag acg cag atc ggc 262
Phe Pro Pro Pro Val Pro Asn Pro Phe Val Gln Gln Thr Gln Ile Gly

40 45 50

tcc gcg agg cgg gtc cag att gtc ctt ctt ggg att atc ttg ctt cca 310
Ser Ala Arg Arg Val Gln Ile Val Leu Leu Gly Ile Ile Leu Leu Pro

55 60 65

att cgt gtc tta ttg gtt gcg tta att tta tta ctt gca tgg cca ttt 358

Ile Arg Val Leu Leu Val Ala Leu Ile Leu Leu Leu Ala Trp Pro Phe

70 75 80

gct gca att tca aca gta tgc tgt cct gaa aag ctg acc cac cca ata 406

	Ala	Ala	Ile	Ser	Thr	Val	Cys	Cys	Pro	Glu	Lys	Leu	Thr	His	Pro	Ile	
		85					90					95					
	act	ggt	tgg	agg	agg	aaa	att	act	caa	aca	gct	ttg	aaa	ttt	ctg	ggt	454
	Thr	Gly	Trp	Arg	Arg	Lys	Ile	Thr	Gln	Thr	Ala	Leu	Lys	Phe	Leu	Gly	
5	100					105					110					115	
	cgt	gct	atg	ttc	ttt	tca	atg	gga	ttt	ata	gtt	gct	gta	aaa	gga	aag	502
	Arg	Ala	Met	Phe	Phe	Ser	Met	Gly	Phe	Ile	Val	Ala	Val	Lys	Gly	Lys	
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	aca	ttc	ttt	gat	gga	att	gcc	tgt	gtt	gta	gct	ggg	tta	cct	tct	ata	598
	Thr	Phe	Phe	Asp	Gly	Ile	Ala	Cys	Val	Val	Ala	Gly	Leu	Pro	Ser	Ile	
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	Val		Arg	Asn	Glu	Asn	Ala	Gln	Val	Pro	Leu	Ile	Gly	Arg	Leu	Leu	
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							ttg									_	694
		Ala	Val	Gln	Pro	Val	Leu	Val	Ser	Arg	Val	Asp	Pro	Asp	Ser	Arg	
20	180					185					190					195	
							ata										742
	Lys	Asn	Thr	Ile		Glu	Ile	Ile	Lys	Arg	Thr	Thr	Ser	Gly	Gly	Glu	
					200					205					210		
25							ttc										790
25	Trp	Pro	Gln	Ile	Leu	Val	Phe	Pro	Glu	Glv	Thr	Cvs	Thr	Asn	Arσ	Ser	

				215					220					225			
	tgt	ttg	att	act	ttt	aaa	cca	gga	gcc	ttc	att	cca	gga	gtt	cca	gtg	838
	Cys	Leu	Ile	Thr	Phe	Lys	Pro	Gly	Ala	Phe	Ile	Pro	Gly	Val	Pro	Val	
			230					235					240				
5	cag	cca	gtc	ctc	ctc	aga	tac	cca	aac	aag	ctg	gat	act	gtg	acc	tgg	886
	Gln	Pro	Val	Leu	Leu	Arg	Tyr	Pro	Asn	Lys	Leu	Asp	Thr	Val	Thr	Trp	
		245					250					255					
	aca	tgg	caa	gga	tat	aca	ttc	att	cag	ctt	tgt	atg	ctt	act	ttc	tgc	934
	Thr	Trp	Gln	Gly	Tyr	Thr	Phe	Ile	Gln	Leu	Cys	Met	Leu	Thr	Phe	Cys	
LO	260					265					270					275	
	cag	ctc	ttc	aca	aag	gta	gaa	gtt	gag	atg	ttt	ctg	ttc	ttt	tgg	gaa	982
	Gln	Leu	Phe	Thr	Lys	Val	Glu	Val	Glu	Met	Phe	Leu	Phe	Phe	Trp	Glu	
					28.0					285					290		
	gga	agc	agc	aag	cat	tgt	tta	aaa	ata	tct	tcc	ttc	ttt	tgc	att	ttt	1030
L5	Gly	Ser	Ser	Lys	His	Cys	Leu	Lys	Ile	Ser	Ser	Phe	Phe	Cys	Ile	Phe	
				295					300					305			
	tct	ctt	cga	aga	ttt	aaa	aga	aga	att	aca	caa	aga	act	aga	act	gca	1078
	Ser	Leu	Arg	Arg	Phe	Lys	Arg	Arg	Ile	Thr	Gln	Arg	Thr	Arg	Thr	Ala	
			310					315					320				
20	cat	ttg	tta	aga	ttg	tcc	ttt	taa	aatt	attt	tc t	gtta	caag	gg aa	aaaa	taaa	1132
	His	Leu	Leu	Arg	Leu	Ser	Phe										
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255/346

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<212> DNA

<213> Homo sapiens

5 <220>

<221> CDS

<222> (71)..(1123)

<400> 115

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Met Ala Leu Pro Pro Gly Pro Ala Ala Leu Arg His Thr

1 5 10

ctg ctg ctc ctg cca gcc ctt ctg agc tca ggt ggg cct ggc acc ccc 157

Leu Leu Leu Leu Pro Ala Leu Leu Ser Ser Gly Gly Pro Gly Thr Pro

15 20 25

aga ttg gcc tgg tat ctg gat gga cag ctg cag gag gcc agc acc tca 205

Arg Leu Ala Trp Tyr Leu Asp Gly Gln Leu Gln Glu Ala Ser Thr Ser

30 35 40 45

20 aga ctg ctg agc gtg gga ggg gag gcc ttc tct gga ggc acc agc acc 253

Arg Leu Leu Ser Val Gly Gly Glu Ala Phe Ser Gly Gly Thr Ser Thr

50 55 60

ttc act gtc act gcc cat cgg gcc cag cat gag ctc aac tgc tct ctg 301 Phe Thr Val Thr Ala His Arg Ala Gln His Glu Leu Asn Cys Ser Leu

25 65 70 75

	cag	gac	ccc	aga	agt	ggc	cga	tca	gcc	aac	gcc	tct	gtc	atc	ctt	aat	349
	Gln	Asp	Pro	Arg	Ser	Gly	Arg	Ser	Ala	Asn	Ala	Ser	Val	Ile	Leu	Asn	
			80					85					90				
	gtg	caa	ttc	aag	cca	gag	att	gcc	caa	gtc	ggc	gcc	aag	tac	cag	gaa	397
5	Val	Gln	Phe	Lys	Pro	Glu	Ile	Ala	Gln	Val	Gly	Ala	Lys	Tyr	Gln	Glu	
		95					100					105					
	gct	cag	ggc	cca	ggc	ctc	ctg	gtt	gtc	ctg	ttt	gcc	ctg	gtg	cgt	gcc	445
	Ala	Gln	Gly	Pro	Gly	Leu	Leu	Val	Val	Leu	Phe	Ala	Leu	Val	Arg	Ala	
	110					115					120					125	
10	aac	ccg	ccg	gcc	aat	gtc	acc	tgg	atc	gac	cag	gat	ggg	cca	gtg	act	493
	Asn	Pro	Pro	Ala	Asn	Val	Thr	Trp	Ile	Asp	Gln	Asp	Gly	Pro	Val	Thr	
					130					135					140		
	gtc	aac	acc	tct	gac	ttc	ctg	gtg	ctg	gat	gcg	cag	aac	tac	ccc	tgg	541
	Val	Asn	Thr	Ser	Asp	Phe	Leu	Val	Leu	Asp	Ala	Gln	Asn	Tyr	Pro	Trp	
15				145					150					155			
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	Leu	Thr	Asn	His	Thr	Val	Gln	Leu	Gln	Leu	Arg	Ser	Leu	Ala	His	Asn	
			160					165					170				
	ctc	tcg	gtg	gtg	gcc	acc	aat	gac	gtg	ggt	gtc	acc	agt	gcg	tcg	ctt	637
20	Leu	Ser	Val	Val	Ala	Thr	Asn	Asp	Val	Gly	Val	Thr	Ser	Ala	Ser	Leu	
		175					180					185					
	cca	gcc	cca	ggg	ctt	ctg	gct	acc	cgg	gtg	gaa	gtg	cca	ctg	ctg	ggc	685
	Pro	Ala	Pro	Gly	Leu	Leu	Ala	Thr	Arg	Val	Glu	Val	Pro	Leu	Leu	Gly	
	190					195					200					205	
25	att	gtt	gtg	gct	gct	ggg	ctt	gca	ctg	ggc	acc	ctc	gtg	ggg	ttc	agc	733

	Ile	Val	Val	Ala	Ala	Gly	Leu	Ala	Leu	Gly	Thr	Leu	Val	Gly	Phe	Ser	
					210					215					220		
	acc	ttg	gtg	gcc	tgc	ctg	gtc	tgc	aga	aaa	gag	aag	aaa	acc	aaa	ggc	781
	Thr	Leu	Val	Ala	Cys	Leu	Val	Cys	Arg	Lys	Glu	Lys	Lys	Thr	Lys	Gŀy	
5				225					230					235			
	ccc	tcc	cgg	cac	cca	tct	ctg	ata	tca	agt	gac	tcc	aac	aac	cta	aaa	829
	Pro	Ser	Arg	His	Pro	Ser	Leu	Ile	Ser	Ser	Asp	Ser	Asn	Asn	Leu	Lys	
			240					245					250				
	ctc	aac	aac	gtg	cgc	ctg	cca	cgg	gag	aac	atg	tcc	ctc	ccg	tcc	aac	877
10	Leu	Asn	Asn	Val	Arg	Leu	Pro	Arg	Glu	Asn	Met	Ser	Leu	Pro	Ser	Asn	
		255					260					265					
	ctt	cag	ctc	aat	gac	ctc	act	cca	gat	tcc	aga	gca	gtg	aaa	cca	gca	925
	Leu	Gln	Leu	Asn	Asp	Leu	Thr	Pro	Asp	Ser	Arg	Ala	Val	Lys	Pro	Ala	
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15	gac	cgg	cag	atg	gct	cag	aac	aac	agc	cgg	cca	gag	ctt	ctg	gac	ccg	973
	Asp	Arg	Gln	Met	Ala	Gln	Asn	Asn	Ser	Arg	Pro	Glu	Leu	Leu	Asp	Pro	
					290					295					300		
	gag	ccc	ggc	ggc	ctc	ctc	acc	agc	caa	gca	tgt	ctc	ctc	cac	cac	ggg	1021
	Glu	Pro	Gly	Gly	Leu	Leu	Thr	Ser	Gln	Ala	Cys	Leu	Leu	His	His	Gly	
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	Thr	Pro	Ala	Leu	Thr	Asn	Pro	Trp	Leu	Pro	His	Gln	Gln	Glu	Gly	Ala	
			320	ļ				325					330	t			
	ctt	cct	gga	gga	tgg	tcg	cca	cag	gca	cat	aat	. tca	aca	gtg	tgg	aag	1117
25	Leu	Pro	Gly	Gly	Trp	Ser	Pro	Gln	Ala	His	Asn	Ser	Thr	val	Trp	Lys	

258/346

335 340 345

ctt tag gggaacatgg agaaagaagg agaccacata ccccaaagtg acctaagaac 1173

Leu 350

actttaaaaa gcaacatgta aatgattgga aattaatata gtacagaata tattttccc 1233
ttgttgagat cttcttttgt aatgtttttc atgttactgc ctagggcggt gctgagcaca 1293
cagcaagttt aataaacttg actgaattca tttaat 1329

<210> 116

10 <211> 1387

<212> DNA

<213> Homo sapiens

<220>

15 <221> CDS

<222> (147)..(488)

<400> 116

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20 ggggctgcct ggcatctggg ggcctcctca gagccagggc tctttctggt tgaggctgag 120

actcactggt gtcatcaggc ccctcc atg aat gag aca aac aaa aca ctt gtt 173

Met Asn Glu Thr Asn Lys Thr Leu Val

5

ggg cct tcg gag ctc ccc aca gcg tct gct gtg gcc cct ggc cca ggc 221

25 Gly Pro Ser Glu Leu Pro Thr Ala Ser Ala Val Ala Pro Gly Pro Gly

	10					15					20					25	
	act	ggg	gct	cgg	gca	tgg	cct	gtg	ctg	gta	gga	ttt	gtg	ctg	ggg	gct	269
	Thr	Gly	Ala	Arg	Ala	Trp	Pro	Val	Leu	Val	Gly	Phe	Val	Leu	Gly	Ala	
					30					35					40		
5	gtg	gtc	ctc	tcg	ctc	ctc	att	gca	ctt	gct	gcc	aaa	tgc	cac	ctc	tgc	317
	Val	۷al	Leu	Ser	Leu	Leu	Ile	Ala	Leu	Ala	Ala	Lys	Cys	His	Leu	Cys	
				45					50					55			
	cgc	cga	tac	cat	gcc	agc	tac	cgg	cac	cgc	cca	ctg	cct	gag	aca	gga	365
	Arg	Arg	Tyr	His	Ala	Ser	Tyr	Arg	His	Arg	Pro	Leu	Pro	Glu	Thr	Gly	
10			60					65					70				•
	agg	gga	ggc	cgc	cca	cag	gtg	gct	gaa	gat	gag	gat	gat	gat	ggc	ttc	413
	Arg	Gly	Gly	Arg	Pro	Gln	Val	Ala	Glu	Asp	Glu	Asp	Asp	Asp	Gly	Phe	
		75					80					85					
	atc	gag	gac	aat	tac	att	cag	cct	ggg	act	ggc	gag	ctg	ggg	aca	gag	461
15	Ile	Glu	Asp	Asn	Tyr	Ile	Gln	Pro	Gly	Thr	Gly	Glu	Leu	Gly	Thr	Glu	
	90					95					100					105	
	ggt	ago	agg	gac	cac	ttc	tco	ctc	tga	gct	.ccca	tct	ttag	acco	tc:		508
	Gly	Ser	Arg	Asp	His	Phe	Ser	Leu	ı								
					110	}											
20	ccc	acto	cct	ccat	.gcct	ga c	agct	taag	g ac	agto	gtta	tga	cato	ggg	gcct	tgaacc	568
	tca	ıggga	cag	aggt	.ggct	gg g	gctt	aaag	g tt	ggco	aggg	ato	gagt	caaa	ccc	cacttcc	628
	cto	jacac	tag	ccaç	caaa	ıgt ç	acaa	tgac	c ct	ctct	tgct	caa	ataad	ctct	caad	etgttcc	688
	cto	ctgt	tct	cago	gataa	ag c	caaa	caaa	ıg go	cttga	agtgt	gga	acata	aagg	ccct	ctgtga	748
	tca	tgc	etct	cggc	ctct	tg g	jttt	tttt	c tt	gcct	tcc	c cta	actti	tact	gtc	gaaatca	808
25	ato	ctat	tct	ccct	ccca	acc a	actto	ccat	g ca	agtti	tece	age	gcac	cttt	gct	cacattg	868

### 260/346

10

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<210> 117

<211> 1158

<212> DNA

<213> Homo sapiens

15

<220>

<221> CDS

<222> (130)..(699)

20 <400> 117

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Met Ala Leu Leu Ser Arg Pro Ala Leu Thr Leu Leu Leu

25

1

5

10

	ctc	atg	gcc	gct	gtt	gtc	agg	tgc	cag	gag	cag	gcc	cag	acc	acc	gac	219
	Leu	Met	Ala	Ala	Val	Val	Arg	Cys	Gln	Glu	Gln	Ala	Gln	Thr	Thr	Asp	
	15					20					25		,			30	
	tgg	aga	gcc	acc	ctg	aag	acc	atc	cgg	aac	ggc	gtt	cat	aag	ata	gac	267
5	Trp	Arg	Ala	Thr	Leu	Lys	Thr	Ile	Arg	Asn	Gly	۷al	His	Lys	Ile	Asp	
					35					40	٠				45		
	acg	tac	ctg	aac	gcc	gcc	ttg	gac	ctc	ctg	gga	ggc	gag	gac	ggt	ctc	315
	Thr	Tyr	Leu	Asn	Ala	Ala	Leu	Asp	Leu	Leu	Gly	Gly	Glu	Asp	Gly	Leu	
				50					55					60			
10	tgc	cag	tat	aaa	tgc	agt	gac	gga	tct	aag	cct	ttc	cca	cgt	tat	ggt	363
	Cys	Gln	Tyr	Lys	Cys	Ser	Asp	Gly	Ser	Lys	Pro	Phe	Pro	Arg	Tyr	Gly	
			65					70					75				
	tat	aaa	ccc	tcc	cca	ccg	aat	gga	tgt	ggc	tct	cca	ctg	ttt	ggt	gtt	411
	Tyr	Lys	Pro	Ser	Pro	Pro	Asn	Gly	Cys	Gly	Ser	Pro	Leu	Phe	Gly	Val	
15		80					85					90					
	cat	ctt	aac	att	ggt	atc	cct	tcc	ctg	aca	aag	tgt	tgc	aac	caa	cac	459
	His	Leu	Asn	Ile	Gly	Ile	Pro	Ser	Leu	Thr	Lys	Cys	Cys	Asn	Gln	His	
	95					100					105					110	
	gac	agg	tgc	tat	gaa	acc	tgt	ggc	aaa	agc	aag	aat	gac	tgt	gat	gaa	507
20	Asp	Arg	Cys	Tyr	Glu	Thr	Cys	Gly	Lys	Ser	Lys	Asn	Asp	Суз	Asp	Glu	
					115					120					125		
	gaa	ttc	cag	tat	tgc	ctc	tcc	aag	atc	tgc	cga	gat	gta	cag	aaa	aca	555
	Glu	Phe	Gln	Tyr	Cys	Leu	Ser	Lys	Ile	Cys	Arg	Asp	Val	Gln	Lys	Thr	
				130					135					140			
25	cta	gga	cta	act	cag	cat	gtt	cag	gca	tgt	gaa	aca	aca	gtg	gag	ctc	603

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		145					150					155				
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	Leu Phe	Asp	Ser	Val	Ile	His	Leu	Gly	Cys	Lys	Pro	Tyr	Leu	Asp	Ser	
5	160	•				165					170					
	caa cga	gcc	gca	tgc	agg	tgt	cat	tat	gaa	gaa	aaa	act	gat	ctt	taa	699
	Gln Arg	Ala	Ala	Cys	Arg	Cys	His	Tyr	Glu	Glu	Lys	Thr	Asp	Leu		
	175				180					185					190	
	aggagat	gcc (	gaca	gctaq	gt ga	acaga	atgaa	a gat	ggaa	agaa	cata	aacct	ttt	gacaa	aataac	759
10	taatgtt	ttt	acaa	cataa	aa ad	ctgto	cttat	: ttt	tgtg	gaaa	ggat	ttati	ttt	gagad	ccttaa	819
	aataatt	tat a	atcti	tgato	gt ta	aaaa	cctca	a aag	gcaaa	aaaa	agt	gaggg	gag .	atagi	gaggg	879
	gagggca	cgc i	ttgto	cttct	c ag	ggtat	ctto	ccc	cagca	attg	ctc	cctta	act ·	tagta	atgcca	939
	aatgtct	tga (	ccaat	tatca	aa aa	acaa	agtgo	ttq	yttta	agcg	gaga	aattt	ttg :	aaaa	gaggaa	999
	tatataa	ctc a	aatti	ttcad	ca ad	caca	attta	cca	aaaa	aaag	agat	tcaaa	ata ·	taaaa	attcat	1059
15	cataatg	tct	gttca	aacat	t at	ctta	atttç	g gaa	aato	<b>1</b> 999	aaat	tato	cac f	ttaca	agtat	1119
•	ttgttta	cta 1	tgaaa	attt	a aa	taca	acatt	: tat	gcct	ag						1158
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	<210> 1	18														
	<211> 1	106														

<220>

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<221> CDS

<212> DNA

<213> Homo sapiens

25 <222> (26)..(859)

### 263/346

<400> 118

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5								1				5					
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	Glu	Leu	Gln	Asp	Thr	Суѕ	Thr	Ser	Leu	Gly	Leu	Met	Leu	Ser	Val	Val	
	10					15	÷				20					25	
	ctg	ctc	atg	ggg	ctg	gcc	cgc	gta	gtc	gcc	cgg	cag	cag	ctg	cac	agg	148
10	Leu	Leu	Met	Gly	Leu	Ala	Arg	Val	Val	Ala	Arg	Gln	Gln	Leu	His	Arg	
					30					35					40		
	ccg	gtg	gcc	cac	gcc	ttc	gtc	ctg	gag	ttt	cta	gcc	acc	ttc	cag	ctc	196
	Pro	Val	Ala	His	Ala	Phe	Val	Leu	Glu	Phe	Leu	Ala	Thr	Phe	Gln	Leu	
				45					50					55			
15	tgc	tgc	tgc	acc	cac	gag	ctg	caa	ctg	ctg	agc	gaa	cag	cac	ccc	gcg	244
	Cys	Cys	Cys	Thr	His	Glu	Leu	Gln	Leu	Leu	Ser	Glu	Gln	His	Pro	Ala	
			60					65					70				
	cac	ccc	acc	tgg	acg	ctg	acg	ctc	gtc	tac	ttc	ttc	tcg	ctt	gtg	cat	292
	His	Pro	Thr	Trp	Thr	Leu	Thr	Leu	Val	Tyr	Phe	Phe	Ser	Leu	Val	His	
20		75					80					85					
	ggc	ctg	act	ctg	gtg	ggc	acg	tcc	agc	aac	ccg	tgc	ggc	gtg	atg	atg	340
	Gly	Leu	Thr	Leu	Val	Gly	Thr	Ser	Ser	Asn	Pro	Cys	Gly	Val	Met	Met	
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	cag	atg	atg	ctg	ggg	ggc	atg	tcc	ccc	gag	acg	ggt	gcg	gtg	agg	cta	388
25	Gln	Met	Met	Leu	Gly	Gly	Met	Ser	Pro	Glu	Thr	Gly	Ala	Val	. Arg	Leu	

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	ttg	gct	cag	ctg	gtt	agt	gcc	ctg	tgc	agc	agg	tac	tgc	aca	agc	gcc	436
	Leu	Ala	Gln	Leu	Val	Ser	Ala	Leu	Cys	Ser	Arg	Tyr	Cys	Thr	Ser	Ala	
				125					130					135			
5	ttg	tgg	agc	ttg	ggt	ctg	acc	cag	tat	cac	gtc	agc	gag	agg	agc	ttc	484
	Leu	Trp	Ser	Leu	Gly	Leu	Thr	Gln	Tyr	His	Val	Ser	Glu	Arg	Ser	Phe	
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	gct	tgc	aag	aat	ccc	atc	cga	gtc	gac	ttg	ctc	aaa	gcg	gtc	atc	aca	532
	Ala	Cys	Lys	Asn	Pro	Ile	Arg	Val	Asp	Leu	Leu	Lys	Ala	Val	Ile	Thr	
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	Glu	Ala	Val	Cys	Ser	Phe	Leu	Phe	His	Ser	Ala	Leu	Leu	His	Phe	Gln	
	170					175					180					185	
	gaa	gtc	cga	acc	aag	ctt	cgt	atc	cac	ctg	ctg	gct	gca	ctc	atc	acc	628
15	Glu	Val	Arg	Thr	Lys	Leu	Arg	Ile	His	Leu	Leu	Ala	Ala	Leu	Ile	Thr	
					190					195					200		
	ttt	ttg	gtc	tat	gca	gga	gga	agt	cta	aca	gga	gct	gta	ttt	aat	cca	676
	Phe	Leu	Val	Tyr	Ala	Gly	Gly	Ser	Leu	Thr	Gly	Ala	Val	Phe	Asn	Pro	
				205					210					215			
20	gct	ttg	gca	ctt	tcg	cta	cat	ttc	atg	tgt	ttt	gat	gaa	gca	ttc	cct	724
	Ala	Leu	Ala	Leu	Ser	Leu	His	Phe	Met	Cys	Phe	Asp	Glu	Ala	Phe	Pro	
			220					225					230				
	cag	ttt	ttt	ata	gta	tac	tgg	ctg	gct	cct	tct	tta	ggt	ata	ttg	ttg	772
	Gln	Phe	Phe	Ile	Val	Tyr	Trp	Leu	Ala	Pro	Ser	Leu	Gly	Ile	Leu	Leu	
25		235					240					245					

265/346

atg att ttg atg ttc agc ttt ttc cat ggc tgc ata aca acc ata caa 820

Met Ile Leu Met Phe Ser Phe Phe His Gly Cys Ile Thr Thr Ile Gln

250 255 260 265

tta ata aaa agg aat aac tgt tcc aaa gac tca gac taa catacaggac 869
Leu Ile Lys Arg Asn Asn Cys Ser Lys Asp Ser Asp

270 275

agtecagetg gatgtgataa agattttate aceteatatg gaaaacaceg getgeaetgg 929
atteateagt gttaaettee tttgaggaag etgeettata gtttteatea etgggaettt 989
aaaaaaaaat taetgtgaaa atgaggtatt etgtaettet eagttaagae ttgttetttg 1049
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<210> 119

<211> 1907

<212> DNA

15 <213> Homo sapiens

<220>

<221> CDS

<222> (159)..(983)

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<400> 119

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25

Met Gly Lys Ser Leu Ser

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	cat	ttg	cct	ttg	cat	tca	agc	aaa	gaa	gat	gct	tat	gat	gga	gtc	aca	224
	His	Leu	Pro	Leu	His	Ser	Ser	Lys	Glu	Asp	Ala	Tyr	Asp	Gly	Val	Thr	
				10					15					20			
5	tct	gaa	aac	atg	agg	aat	gga	ctg	gtt	aat	agt	gaa	gtc	cat	aat	gaa	272
	Ser	Glu	Asn	Met	Arg	Asn	Gly	Leu	Val	Asn	Ser	Glu	Val	His	Asn	Glu	
			25					30					35				
	gat	gga	aga	aat	gga	gat	gtc	tct	cag	ttt	cca	tat	gtg	gaa	ttt	aca	320
	Asp	Gly	Arg	Asn	Gly	Asp	Val	Ser	Gln	Phe	Pro	Tyr	Val	Glu	Phe	Thr	
LO		40					45					50					
	gga	aga	gat	agt	gtc	acc	tgc	cct	act	tgt	cag	gga	aca	gga	aga	att	368
	Gly	Arg	Asp	Ser	Val	Thr	Cys	Pro	Thr	Cys	Gln	Gly	Thr	Gly	Arg	Ile	
	55					60					65					70	
	cct	agg	ggg	caa	gaa	aac	caa	ctg	gtg	gca	ttg	att	cca	tat	agt	gat	416
1.5	Pro	Arg	Gly	Gln	Glu	Asn	Gln	Leu	Val	Ala	Leu	Ile	Pro	Tyr	Ser	Asp	
					75					80					85		
	cag	aga	tta	agg	cca	aga	aga	aca	aag	ctg	tat	gtg	atg	gct	tct	gtg	464
	Gln	Arg	Leu	Arg	Pro	Arg	Arg	Thr	Lys	Leu	Tyr	Val	Met	Ala	Ser	Val	
				90					95					100			
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	Phe	۷al	Cys	Leu	Leu	Leu	Ser	Gly	Leu	Ala	Val	Phe	Phe	Leu	Phe	Pro	
			105					110					115				
	cgc	tct	atc	gac	gtg	aaa	tac	att	ggt	gta	aaa	tca	gcc	tat	gtc	agt	560
	Arg	Ser	Ile	Asp	Val	Lys	Tyr	Ile	Gly	Val	Lys	Ser	Ala	Tyr	Val	Ser	
25		120					125					120					

	tat	gat	gtt	cag	aag	cgt	aca	att	tat	tta	aat	atc	aca	aac	aca	cta	608
	Tyr	Asp	Val	Gln	Lys	Arg	Thr	Ile	Tyr	Leu	Asn	Ile	Thr	Asn	Thr	Leu	
	135					140					145					150	
	aat	ata	aca	aac	aat	aac	tat	tac	tct	gtc	gaa	gtt	gaa	aac	atc	act	656
5	Asn	Ile	Thr	Asn	Asn	Asn	Tyr	Tyr	Ser	Val	Glu	Val	Glu	Asn	Ile	Thr	
					155					160					165		
	gcc	caa	gtt	caa	ttt	tca	aaa	aca	gtt	att	gga	aag	gca	cgc	tta	aac	704
	Ala	Gln	Val	Gln	Phe	Ser	Lys	Thr	Val	Ile	Gly	Lys	Ala	Arg	Leu	Asn	
				170					175					180			
10	aac	ata	acc	att	att	ggt	cca	ctt	gat	atg	aaa	caa	att	gat	tac	aca	752
	Asn	Ile	Thr	Ile	Ile	Gly	Pro	Leu	Asp	Met	Lys	Gln	Ile	Asp	Tyr	Thr	
			185					190					195				
	gta	cct	acc	gtt	ata	gca	gag	gaa	atg	agt	tat	atg	tat	gat	ttc	tgt	800
	Val	Pro	Thr	Val	Ile	Ala	Glu	Glu	Met	Ser	Tyr	Met	Tyr	Asp	Phe	Cys	
15		200					205					210					
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	Thr	Leu	Ile	Ser	Ile	Lys	Val	His	Asn	Ile	Val	Leu	Met	Met	Gln	Val	
	215					220					225					230	
	act	gtg	aca	aca	aca	tac	ttt	ggc	cac	tct	gaa	cag	ata	tcc	cag	gag	896
20	Thr	Val	Thr	Thr	Thr	Tyr	Phe	Gly	His	Ser	Glu	Gln	Ile	Ser	Gln	Glu	
					235					240	ı				245		
	agg	tat	. cag	tat	gto	gac	tgt	gga	aga	.aac	aca	act	tat	cag	ttg	ggg	944
	Arg	Tyr	Gln	Tyr	Val	Asp	Cys	Gly	Arg	Asn	Thr	Thr	Tyr	Gln	Leu	Gly	
				250					255					260	)		
25	cag	tct	gaa	tat	tta	aat	gta	ctt	cag	CC	caa	caç	r taa	aaa	ctgg	aag	993

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Gln Ser Glu Tyr Leu Asn Val Leu Gln Pro Gln Gln

265 270 275

agatggattt aaagaagaaa tatctattga tatttcctat actctcaatg aagaggtatt 1053 tcctaatagg agaccttaaa ttgaacaaac ctaaagttta cacttctaag agtacagtta 1113 aaagtatgtg gacctgcagt tcttgtaact ctccactctg tgttaatgat atatttgtac 1173 taggatettt taettgaate taaatttaet ggttgattte ettetecage etateceeta 1233 cagggaaaag ctgatacttc ccctatagta caataaataa ttatttaaaa gtcatagctc 1293 cagtcactac tgaaaacata attttggtga taaaataatt tgagaaactt aatttctgaa 1353 tgtttttata gaaaattact gaaagtctat tactcatgga agacttttaa agaataacct 1413 tttttcctgt tttataaatt cccattgtta tatggtagta tttcagctac acaatatttt 1473 agcttttagc tagacattta tagcttttca tttgttgaaa tggtaatcat ctgcatgttt 1533 ttgtcactta tttcaggtta gtgattgcct aacacttata agccaaaata atctttgcaa 1593 aattccatac ctaaaatttt gaaagcccct aatgttttca cacatctttc tgtattagtt 1653 atagtittgt gaaatetttg tgtgatette aaacattate atttaatgta caatactgta 1713 aataaactgt gcatggcttt tatacagctt tagtaaatgt caaataaagt ggtacagact 1773 cattacaaca agtttctcat aaaaaatacaa taaataggaa aatgaaattc agaaacccat 1833 agactgggaa taggttccag ttacagcttg gatctggcat aaaataaatt tgaaataaaa 1893 tattttgatg ctcc 1907

20 <210> 120

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<211> 1816

<212> DNA

<213> Homo sapiens

25 <220>

### 269/346

<221> CDS

<222> (134)..(1306)

<400> 120

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gccagggagg gcc atg att tcc ctc ccg ggg ccc ctg gtg acc aac ttg 169
Met Ile Ser Leu Pro Gly Pro Leu Val Thr Asn Leu

1 5 10

ctg cgg ttt ttg ttc ctg ggg ctg agt gcc ctc gcg ccc ccc tcg cgg 217

Leu Arg Phe Leu Phe Leu Gly Leu Ser Ala Leu Ala Pro Pro Ser Arg

15 20 25

gcc cag ctg caa ctg cac ttg ccc gcc aac cgg ttg cag gcg gtg gag 265 Ala Gln Leu Gln Leu His Leu Pro Ala Asn Arg Leu Gln Ala Val Glu

15 30 35 40

gga ggg gaa gtg gtg ctt cca gcg tgg tac acc ttg cac ggg gag gtg 313 Gly Gly Glu Val Val Leu Pro Ala Trp Tyr Thr Leu His Gly Glu Val

45 50 55 60

tct tca tcc cag cca tgg gag gtg ccc ttt gtg atg tgg ttc ttc aaa 361

20 Ser Ser Ser Gln Pro Trp Glu Val Pro Phe Val Met Trp Phe Phe Lys

65 70 75

Cag aaa gaa aag gag gat cag gtg ttg tcc tac atc aat ggg gtc aca 409
Gln Lys Glu Lys Glu Asp Gln Val Leu Ser Tyr Ile Asn Gly Val Thr

80 85 90

aca age aaa cet gga gta tee ttg gte tae tee atg eee tee egg aac 457

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	ctg	tcc	ctg	cgg	ctg	gag	ggt	ctc	cag	gag	aaa	gac	tct	ggc	ccc	tac	505
	Leu	Ser	Leu	Arg	Leu	Glu	Gly	Leu	Gln	Glu	Lys	Asp	Ser	Gly	Pro	Tyr	
5		110					115					120					
	agc	tgc	tcc	gtg	aat	gtg	caa	gac	aaa	caa	ggc	aaa	tct	agg	ggc	cac	553
	Ser	Cys	Ser	Val	Asn	Val	Gln	Asp	Lys	Gln	Gly	Lys	Ser	Arg	Gly	His	
	125					130					135					140	
	agc	atc	aaa	acc	tta	gaa	ctc	aat	gta	ctg	gtt	cct	cca	gct	cct	cca	601
10	Ser	Ile	Lys	Thr	Leu	Glu	Leu	Asn	Val	Leu	Val	Pro	Pro	Ala	Pro	Pro	
					145					150					155		
	tcc	tgc	cgt	ctc	cag	ggt	gtg	ccc	cat	gtg	ggg	gca	aac	gtg	acc	ctg	649
	Ser	Cys	Arg	Leu	Gln	Gly	Val	Pro	His	Val	Gly	Ala	Asn	Val	Thr	Leu	
				160					165					170			
15	agc	tgc	cag	tct	cca	agg	agt	aag	ccc	gct	gtc	caa	tac	cag	tgg	gat	697
	Ser	Cys	Gln	Ser	Pro	Arg	Ser	Lys	Pro	Ala	Val	Gln	Tyr	Gln	Trp	Asp	
			175					180					185				
	cgg	cag	ctt	cca	tcc	ttc	cag	act	ttc	ttt	gca	cca	gca	tta	gat	gtc	745
	Arg	Gln	Leu	Pro	Ser	Phe	Gln	Thr	Phe	Phe	Ala	Pro	Ala	Leu	Asp	Val	
20		190					195					200					
	atc	cgt	ggg	tct	tta	agc	ctc	acc	aac	ctt	tcg	tct	tcc	atg	gct	gga	793
	Ile	Arg	Gly	Ser	Leu	Ser	Leu	Thr	Asn	Leu	Ser	Ser	Ser	Met	Ala	Gly	
	205					210					215					220	
	gtc	tat	gtc	tgc	aag	gcc	cac	aat	gag	gtg	ggc	act	gcc	caa	tgt	aat	841
25	Val	Tyr	Val	Cys	Lys	Ala	His	Asn	Glu	Val	Gly	Thr	Ala	Gln	Cys	Asn	•

					225					230					235		
	gtg	acg	ctg	gaa	gtg	agc	aca	ggg	cct	gga	gct	gca	gtg	gtt	gct	gga	889
	Val	Thr	Leu	Glu	Val	Ser	Thr	Gly	Pro	Gly	Ala	Ala	Val	Val	Ala	Gly	
				240					245					250			
5	gct	gtt	gtg	ggt	acc	ctg	gtt	gga	ctg	ggg	ttg	ctg	gct	ggg	ctg	gtc	937
	Ala	Val	Val	Gly	Thr	Leu	Val	Gly	Leu	Gly	Leu	Leu	Ala	Gly	Leu	Val	
			255					260					265				
	ctc	ttg	tac	cac	tgc	cgg	ggc	aag	gcc	ctg	gag	gag	cca	gcc	aat	gat	985
	Leu	Leu	Tyr	His	Cys	Arg	Gly	Lys	Ala	Leu	Glu	Glu	Pro	Ala	Asn	Asp	
10		270					275					280					
	atc	aag	gag	gat	gcc	att	gct	ccc	cgg	acc	ctg	ccc	tgg	ccc	aag	agc	1033
	Ile	Lys	Glu	Asp	Ala	Ile	Ala	Pro	Arg	Thr	Leu	Pro	Trp	Pro	Lys	Ser	
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15	Ser	Asp	Thr	Ile	Ser	Lys	Asn	Gly	Thr	Leu	Ser	Ser	Val	Thr	Ser	Ala	
					305					310					315		
	cga	gcc	ctc	cgg	cca	ccc	cat	ggc	cct	ccc	agg	cct	ggt	gca	ttg	acc	1129
	Arg	Ala	Leu	Arg	Pro	Pro	His	Gly	Pro	Pro	Arg	Pro	Gly	Ala	Leu	Thr	
				320					325					330			
20	ccc	acg	ccc	agt	ctc	tcc	agc	cag	gcc	ctg	ccc	tca	cca	aga	ctg	ccc	1177
	Pro	Thr	Pro	Ser	Leu	Ser	Ser	Gln	Ala	Leu	Pro	Ser	Pro	Arg	Leu	Pro	
			335					340					345				
	acg	aca	gat	ggg	gcc	cac	cct	caa	cca	ata	tcc	ccc	atc	cct	ggt	ggg	1225
	Thr	Thr	Asp	Gly	Ala	His	Pro	Gln	Pro	Ile	Ser	Pro	Ile	Pro	Gly	Gly	
25		350					355					360					

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gtt tct tcc tct ggc ttg agc cgc atg ggt gct gtg cct gtg atg gtg 1273

Val Ser Ser Ser Gly Leu Ser Arg Met Gly Ala Val Pro Val Met Val

365 370 375 380

cct gcc cag agt caa gct ggc tct ctg gta tga tgaccccacc actcattggc 1326 Pro Ala Gln Ser Gln Ala Gly Ser Leu Val

385 390

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aaaceatete agtaagaeet aagtgteeag gagacagaag gagaagagga agtggatetg 1506
gaattgggag gageeteeae eeaceeetga eteeteetta tgaageeage tgetgaaatt 1566
agetaeteae eaagagtgag gggeagagae tteeagteae tgagteteee aggeeeeett 1626
gatetgtaee eeaceeetat etaacaeeae eettggetee eacteeaget eeetgtattg 1686
atataaeetg teaggetgge ttggttaggt tttaetgggg eagaggatag ggaatetett 1746
attaaaaeta acatgaaata tgtgttgttt teatttgeaa atttaaataa agatacataa 1806
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<210> 121

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15

<211> 395

<212> PRT

20 <213> Homo sapiens

<400> 121

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	Ala	Ala	Thr	Val	Gln	Ser	Arg	Gly	Gln	Tyr	Ser	Суѕ	Ser	Gly	Gln	Val
			35					40					45			
	Met	Tyr	Ile	Pro	Gln	Thr	Phe	Thr	Gln	Thr	Ser	Glu	Thr	Ala	Met	Val
5		50					55					60				
	Gln	Val	Gln	Glu	Leu	Phe	Pro	Pro	Pro	Val	Leu	Ser	Ala	Ile	Pro	Ser
	65					70					75					80
	Pro	Glu	Pro	Arg	Glu	Gly	Ser	Leu	Val	Thr	Leu	Arg	Суѕ	Gln	Thr	Lys
					85					90					95	
10	Leu	His	Pro	Leu	Arg	Ser	Ala	Leu	Arg	Leu	Leu	Phe	Ser	Phe	His	Lys
				100					105					110		
	Asp	Gly	His	Thr	Leu	Gln	Asp	Arg	Gly	Pro	His	Pro	Glu	Leu	Cys	Il∈
		•	115					120					125			
	Pro	Gly	Ala	Lys	Glu	Gly	Asp	Ser	Gly	Leu	Tyr	Trp	Cys	Glu	Val	Ala
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	Pro	Glu	Gly	Gly	Gln	Val	Gln	Lys	Gln	Ser	Pro	Gln	Leu	Glu	Val	Arg
	145					150					155					160
	Val	Gln	Ala	Pro	Val	Ser	Arg	Pro	Val	Leu	Thr	Leu	His	His	Gly	Pro
					165					170					175	
20	Ala	Asp	Pro	Ala	Val	Gly	Asp	Met	Val	Gln	Leu	Leu	Суз	Glu	Ala	Glr
				180					185					190		
	Arg	Gly	Ser	Pro	Pro	Ile	Leu	Tyr	Ser	Phe	Tyr	Leu	Asp	Glu	Lys	Ile
			195					200					205			
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25		210					215					220				

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5	Gly	Ser	Gln	Val	Leu	Phe	Thr	Pro	Ala	Ser	Asn	Trp	Leu	Val	Pro	Trp
				260					265					270		
	Leu	Pro	Ala	Ser	Leu	Leu	Gly	Leu	Met	Val	Ile	Ala	Ala	Ala	Leu	Leu
			275					280					285			
	Val	Tyr	Val	Arg	Ser	Trp	Arg	Lys	Ala	Gly	Pro	Leu	Pro	Ser	Gln	Ile
10		290					295					300				
	Pro	Pro	Thr	Ala	Pro	Gly	Gly	Glu	Gln	Cys	Pro	Leu	Tyr	Ala	Asn	Val
	305					310					315					320
	His	His	Gln	Lys	Gly	Lys	Asp	Glu	Gly	Val	Val	Tyr	Ser	Val	Val	His
					325					330					335	-
15	Arg	Thr	Ser	Lys	Arg	Ser	Glu	Ala	Arg	Ser	Ala	Glu	Phe	Thr	Val	Gly
				340					345					350		
	Arg	Lys	Asp	Ser	Ser	Ile	Ile	Cys	Ala	Glu	Val	Arg	Cys	Leu	Gln	Pro
			355					360		•			365			
	Ser	Glu	Val	Ser	Ser	Thr	Glu	Val	Asn	Met	Arg	Ser	Arg	Thr	Leu	Gln
20		370	•				375					380				
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<210> 122

25 <211> 550

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<212> PRT

<213> Homo sapiens

	<400	0> 12	22													
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	1				5					10					15	
	Gln	Thr	Leu	Gln	Val	Leu	Thr	Phe	Ile	Leu	Pro	Cys	Leu	Met	Ile	Pro
				20					25					30		
	Ser	Gln	Met	Leu	Leu	Glu	Asn	Phe	Ser	Ala	Ala	Ile	Pro	Gly	His	Arg
10			35					40					45			
	Cys	Trp	Thr	His	Met	Leu	Asp	Asn	Gly	Ser	Ala	Val	Ser	Thr	Asn	Met
		50					55					60				
	Thr	Pro	Lys	Ala	Leu	Leu	Thr	Ile	Ser	Ile	Pro	Pro	Gly	Pro	Asn	Gln
	65					70					75					80
15	Gly	Pro	His	Gln	Cys	Arg	Arg	Phe	Arg	Gln	Pro	Gln	Trp	Gln	Leu	Leu
					85					90					95	
	Asp	Pro	Asn	Ala	Thr	Ala	Thr	Ser	Trp	Ser	Glu	Ala	Asp	Thr	Glu	Pro
				100					105					110		
	Cys	Val	Asp	Gly	Trp	Val	Tyr	Asp	Arg	Ser	Val	Phe	Thr	Ser	Thr	Ile
20			115					120					125			
	Val	Ala	Lys	Trp	Asp	Leu	Val	Cys	Ser	Ser	Gln	Gly	Leu	Lys	Pro	Leu
		130					135					140				
	Ser	Gln	Ser	Ile	Phe	Met	Ser	Gly	Ile	Leu	Val	Gly	Ser	Phe	Ile	Trp
	145					150					155					160
25	Gly	Leu	Leu	Ser	Tyr	Arg	Phe	Gly	Arg	Lys	Pro	Met	Leu	ser	Trp	Cys

					165					170					175	
	Cys	Leu	Gln	Leu	Ala	Val	Ala	Gly	Thr	Ser	Thr	Ile	Phe	Ala	Pro	Thr
				180					185					190		
	Phe	Val	Ile	Tyr	Суѕ	Gly	Leu	Arg	Phe	Val	Ala	Ala	Phe	Gly	Met	Ala
5			195					200					205			
	Gly	Ile	Phe	Leu	Ser	Ser	Leu	Thr	Leu	Met	Val	Glu	Trp	Thr	Thr	Thr
		210					215					220				
	Ser	Arg	Arg	Ala	Val	Thr	Met	Thr	Val	Val	Gly	Cys	Ala	Phe	Ser	Ala
	225					230					235					240
10	Gly	Gln	Ala	Ala	Leu	Gly	Gly	Leu	Ala	Phe	Ala	Leu	Arg	Asp	Trp	Arg
					245					250					255	
	Thr	Leu	Gln	Leu	Ala	Ala	Ser	Val	Pro	Phe	Phe	Ala	Ile	Ser	Leu	Ile
				260					265					270		
	Ser	Trp	Trp	Leu	Pro	Glu	Ser	Ala	Arg	Trp	Leu	Ile	Ile	Lys	Gly	Lys
15			275					280					285			
	Pro	Asp	Gln	Ala	Leu	Gln	Glu	Leu	Arg	Lys	Val	Ala	Arg	Ile	Asn	Gly
		290					295					300				
	His	Lys	Glu	Ala	Lys	Asn	Leu	Thr	Ile	Glu	Val	Leu	Met	Ser	Ser	Val
	305					310					315					320
20	Lys	Glu	Glu	Val	Ala	Ser	Ala	Lys	Glu	Pro	Arg	Ser	Val	Leu	Asp	Leu
					325					330					335	
	Phe	Cys	Val	Pro	Val	Leu	Arg	Trp	Arg	Ser	Cys	Ala	Met	Leu	Val	Val
				340					345					350		
	Asn	Phe	Ser	Leu	Leu	Ile	Ser	Tyr	Tyr	Gly	Leu	Val	Phe	Asp	Leu	Gln
25			355					360					365			

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	Ser	Leu	Gly	Arg	Asp	Ile	Phe	Leu	Leu	Gln	Ala	Leu	Phe	Gly	Ala	Val
		370					375					380				
	Asp	Phe	Leu	Gly	Arg	Ala	Thr	Thr	Ala	Leu	Leu	Leu	Ser	Phe	Leu	Gly
	385					390					395					400
5	Arg	Arg	Thr	Ile	Gln	Ala	Gly	Ser	Gln	Ala	Met	Ala	Gly	Leu	Ala	Ile
					405					410					415	
	Leu	Ala	Asn	Met	Leu	Val	Pro	Gln	Asp	Leu	Gln	Thr	Leu	Arg	Val	Val
				420					425					430		
	Phe	Ala	Val	Leu	Gly	Lys	Gly	Cys	Phe	Gly	Ile	Ser	Leu	Thr	Cys	Leu
10			435					440					445			
	Thr	Ile	Tyr	Lys	Ala	Glu	Leu	Phe	Pro	Thr	Pro	Val	Arg	Met	Thr	Ala
		450	-	-			455					460	-			
	Asp	Gly	Ile	Leu	His	Thr	Val	Gly	Arg	Leu	Gly	Ala	Met	Met	Gly	Pro
	465					470					475					480
15	Leu	Ile	Leu	Met	Ser	Arg	Gln	Ala	Leu	Pro	Leu	Leu	Pro	Pro	Leu	Leu
					485					490					495	
	Tyr	Gly	Val	Ile	Ser	Ile	Ala	Ser	Ser	Leu	Val	Val	Leu	Phe	Phe	Leu
				500					505					510		
	Pro	Glu	Thr	Gln	Gly	Leu	Pro	Leu	Pro	Asp	Thr	Ile	Gln	Asp	Leu	Glu
20			515					520					525			
	Ser	Gln	Lys	Ser	Thr	Ala	Ala	Gln	Gly	Asn	Arg	Gln	Glu	Ala	Val	Thr
		530					535					540				
	Val	Glu	Ser	Thr	Ser	Leu										
	545					550				ē						

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	<21	1> 2	18							,						
	<21	2> P.	RT													
	<21	3> H	omo	sapi	ens											
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	<40	0> 1	23									-				
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`	1				5					10					15	
	Gly	Leu	Ala	Leu	Ser	Gln	Leu	Ala	Ala	Gly	Ala	Thr	Asp	Cys	Lys	Phe
10				20					25					30		
	Leu	Gly	Pro	Ala	Glu	His	Leu	Thr	Phe	Thr	Pro	Ala	Ala	Arg	Ala	Arg
			35					40					45			
	Trp	Leu	Ala	Pro	Arg	Val	Arg	Ala	Pro	Gly	Leu	Leu	Asp	Ser	Leu	Tyr
		50					55					60				
15	Gly	Thr	Val	Arg	Arg	Phe	Leu	Ser	Val	Val	Gln	Leu	Asn	Pro	Phe	Pro
	65					70					75					80
	Ser	Glu	Leu	Val	Lys	Ala	Leu	Leu	Asn	Glu	Leu	Ala	Ser	Val	Lys	Val
					85					90					95	
	Asn	Glu	Val	Val	Arg	Tyr	Glu	Ala	Gly	Tyr	Val	Val	Cys	Ala	Val	Ile
20				100					105					110		
	Ala	Gly	Leu	Tyr	Leu	Leu	Leu	Val	Pro	Thr	Ala	Gly	Leu	Cys	Phe	Cys
			115					120					125			
	Cys	Cys	Arg	Cys	His	Arg	Arg	Cys	Gly	Gly	Arg	Val	Lys	Thr	Glu	His
		130					135					140				
25	Lys	Ala	Leu	Ala	Cys	Glu	Arg	Ala	Ala	Leu	Met	Val	Phe	Leu	Leu	Leu

	145					150					155					160
	Thr	Thr	Leu	Leu	Leu	Leu	Ile	Gly	Val	Val	Cys	Ala	Phe	Val	Thr	Asn
					165					170					175	
	Gln	Arg	Thr	His	Glu	Gln	Met	Gly	Pro	Ser	Ile	Glu	Ala	Met	Pro	Glu
5				180				٠	185					190		
	Thr	Leu	Leu	Ser	Leu	Trp	Gly	Leu	Val	Ser	Asp	Val	Pro	Gln	Val	Ser
			195					200					205			
	Thr	Val	Thr	Pro	His	Pro	His	Val	Pro	Leu						
		210					215									
10																
	<21	0> 1:	24													
	<21	1> 5	96													
	<21	2> P	RT													
	<21	3> H	omo	sapi	ens											
15																
	<40	0> 1	24				•									
	Met	Ala	Ala	Asn	Ser	Thr	Ser	Asp	Leu	His	Thr	Pro	Gly	Thr	Gln	Leu
	1	•			5					10					15	
	Ser	. Val	Ala	Asp	Ile	Ile	. Val	. Ile	Thr	. Val	Tyr	Phe	Ala	Leu	Asn	Val
20				20	)				25	•				30		
	Ala	val	. Gly	7 Ile	Trp	Ser	Ser	: Cys	Arg	, Ala	Ser	Arg	Asr	Thr	Val	Asn
			35	5				40	)				45	5		
	Gly	у Туг	Phe	e Leu	ı Ala	Gl	Arg	J Asp	Met	: Thi	Trp	Trp	Pro	Ile	Gly	Ala
		50	)				55	5				60	)			
25	Sei	Leu	ı Phe	ala e	a Ser	: Sei	c Gli	ı Gly	, Sei	r Gly	Lev	ı Phe	e Ile	e Gly	Let	ı Ala

	65					70					75					80
	Gly	Ser	Gly	Ala	Ala	Gly	Gly	Leu	Ala	Val	Ala	Gly	Phe	Glu	Trp	Asn
					85					90					95	
	Ala	Thr	Tyr	Val	Leu	Leu	Ala	Leu	Ala	Trp	Val	Phe	Val	Pro	Ile	Tyr
5				100					105					110		
	Ile	Ser	Ser	Glu	Ile	Val	Thr	Leu	Pro	Glu	Tyr	Ile	Gln	Lys	Arg	Tyr
			115					120					125			
	Gly	Gly	Gln	Arg	Ile	Arg	Met	Tyr	Leu	Ser	Val	Leu	Ser	Leu	Leu	Leu
		130					135					140				
LO ·	Ser	Val	Phe	Thr	Lys	Ile	Ser	Leu	Asp	Leu	Tyr	Ala	Gly	Ala	Leu	Phe
	145					150					155					160
	Val	His	Ile	Cys	Leu	Gly	Trp	Asn	Phe	Tyr	Leu	Ser	Thr	Ile	Leu	Thr
					165					170					175	
	Leu	Gly	Ile	Thr	Ala	Leu	Tyr	Thr	Ile	Ala	Gly	Gly	Leu	Ala	Ala	Val
L5				180					185					190		
	Ile	Tyr	Thr	Asp	Ala	Leu	Gln	Thr	Leu	Ile	Met	Val	Val	Gly	Ala	Val
			195					200					205			
	Ile	Leu	Thr	Ile	Lys	Ala	Phe	Asp	Gln	Ile	Gly	Gly	Tyr	Gly	Gln	Leu
	,	210					215					220				
20	Glu	Ala	Ala	Tyr	Ala	Gln	Ala	Ile	Pro	Ser	Arg	Thr	Ile	Ala	Asn	Thr
	225					230					235					240
	Thr	Cys	His	Leu	Pro	Arg	Thr	Asp	Ala	Met	His	Met	Phe	Arg	Asp	Pro
					245					250					255	
	His	Thr	Gly		Leu	Pro	Trp	Thr	Gly	Met	Thr	Phe	Gly	Leu	Thr	Ile
25				260					265					270		

	Met	Ala	Thr	Trp	Tyr	Trp	Cys	Thr	Asp	Gln	Val	Ile	Val	Gln	Arg	Ser
			275					280					285			
	Leu	Ser	Ala	Arg	Asp	Leu	Asn	His	Ala	Lys	Ala	Gly	Ser	Ile	Leu	Ala
		290					295					300				
5	Ser	Tyr	Leu	Lys	Met	Leu	Pro	Met	Gly	Leu	Ile	Ile	Met	Pro	Gly	Met
	305					310					315					320
	Ile	Ser	Arg	Ala	Leu	Phe	Pro	Asp	Asp	Val	Gly	Cys	Val	Val	Pro	Ser
					325					330					335	
	Glu	Cys	Leu	Arg	Ala	Суѕ	Gly	Ala	Glu	Val	Gly	Cys	Ser	Asn	Ile	Ala
10				340					345	•				350		•
	Tyr	Pro	Lys	Leu	Val	Met	Glu	Leu	Met	Pro	Ile	Gly	Leu	Arg	Gly	Leu
			355					360					365			
	Met	Ile	Ala	Val	Met	Leu	Ala	Ala	Leu	Met	Ser	Ser	Leu	Thr	Ser	Ile
		370					375					380				
15	Phe	Asn	Ser	Ser	Ser	Thr	Leu	Phe	Thr	Met	Asp	Ile	Trp	Arg	Arg	Leu
	385					390					395					400
	Arg	Pro	Arg	Ser	Gly	Glu	Arg	Glu	Leu	Leu	Leu	Val	Gly	Arg	Leu	Val
					405					410					415	_
	Ile	Val	Ala	Leu	Ile	Gly	Val	Ser	Val	Ala	Trp	Ile	Pro	Val	Leu	Gln
20				420					425					430		
	Asp	Ser	Asn	Ser	Gly	Gln	Leu	Phe	Ile	Tyr	Met	Gln	Ser	Val	Thr	Ser
			435					440					445			
	Ser	Leu	Ala	Pro	Pro	Val	Thr	Ala	Val	Phe	Val	Leu	Gly	Val	Phe	Trp
		450					455					460				
25	Arg	Arg	Ala	Asn	Glu	Gln	Gly	Ala	Phe	Trp	Gly	Leu	Ile	Ala	Gly	Leu

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Val Val Gly Ala Thr Arg Leu Val Leu Glu Phe Leu Asn Pro Ala Pro Pro Cys Gly Glu Pro Asp Thr Arg Pro Ala Val Leu Gly Ser Ile His Tyr Leu His Phe Ala Val Ala Leu Phe Ala Leu Ser Gly Ala Val Val Val Ala Gly Ser Leu Leu Thr Pro Pro Pro Gln Ser Val Gln Ile Glu Asn Leu Thr Trp Trp Thr Leu Ala Gln Asp Val Pro Leu Gly Thr Lys Ala Gly Asp Gly Gln Thr Pro Gln Lys His Ala Phe Trp Ala Arg Val Cys Gly Phe Asn Ala Ile Leu Leu Met Cys Val Asn Ile Phe Tyr Ala Tyr Phe Ala <210> 125 <211> 467 <212> PRT <213> Homo sapiens <400> 125

Met Trp Arg Cys Pro Leu Gly Leu Leu Leu Leu Pro Leu Ala Gly

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	His	Leu	Ala	Leu	Gly	Ala	Gln	Gln	Gly	Arg	Gly	Arg	Arg	Glu	Leu	Ala
				20					25					30		
	Pro	Gly	Leu	His	Leu	Arg	Gly	Ile	Arg	Asp	Ala	Gly	Gly	Arg	Tyr	Cys
5			35					40					45			
	Gln	Glu	Gln	Asp	Leu	Cys	Cys	Arg	Gly	Arg	Ala	Asp	Asp	Cys	Ala	Leu
		50					55		-			60				
	Pro	Tyr	Leu	Gly	Ala	Ile	Суѕ	Tyr	Cys	Asp	Leu	Phe	Cys	Asn	Arg	Thr
	65					70					75					80
10	Val	Ser ·	Asp	Cys	Cys	Pro	Asp	Phe	Trp	Asp	Phe	Cys	Leu	Gly	Val	Pro
					85					90					95	
	Pro	Pro	Phe	Pro	Pro	Ile	Gln	Gly	Cys	Met	His	Gly	Gly	Arg	Ile	Tyr
				100					105					110		
	Pro	Val	Leu	Gly	Thr	Tyr	Trp	Asp	Asn	Cys	Asn	Arg	Cys	Thr	Cys	Gln
15			115					120					125			
	Glu	Asn	Arg	Gln	Trp	Gln	Cys	Asp	Gln	Glu	Pro	Cys	Leu	Val	Asp	Pro
		130					135					140				
	Asp	Met	Ile	Lys	Ala	Ile	Asn	Gln	Gly	Asn	Tyr	Gly	Trp	Gln	Ala	Gly
	145					150					155					160
20	Asn	His	Ser	Ala	Phe	Trp	Gly	Met	Thr	Leu	Asp	Glu	Gly	Ile	Arg	Tyr
					165					170					175	
	Arg	Leu	Gly	Thr	Ile	Arg	Pro	Ser	Ser	Ser	Val	Met	Asn	Met	His	Glu
				180					185					190		
	Ile	Tyr	Thr	Val	Leu	Asn	Pro	Gly	Glu	Val	Leu	Pro	Thr	Ala	Phe	Glu
25			195					200					205			

	Ala	Ser	Glu	Lys	Trp	Pro	Asn	Leu	Ile	His	Glu	Pro	Leu	Asp	Gln	Gly
		210					215					220				
	Asn	Cys	Ala	Gly	Ser	Trp	Ala	Phe	Ser	Thr	Ala	Ala	Val	Ala	Ser	Asp
	225					230				-	235					240
5	Arg	Val	Ser	Ile	His	Ser	Leu	Gly	His	Met	Thr	Pro	Val	Leu	Ser	Pro
					245					250					255	
	Gln	Asn	Leu	Leu	Ser	Cys	Asp	Thr	His	Gln	Gln	Gln	Gly	Cys	Arg	Gly
				260					265					270		
	Gly	Arg	Leu	Asp	Gly	Ala	Trp	Trp	Phe	Leu	Arg	Arg	Arg	Gly	Val	Val
10			275					280					285			
	Ser	Asp	His	Cys	Tyr	Pro	Phe	Ser	Gly	Arg	Glu	Arg	Asp	Glu	Ala	Gly
		290					295					300				•
	Pro	Ala	Pro	Pro	Cys	Met	Met	His	Ser	Arg	Ala	Met	Gly	Arg	Gly	Lys
	305					310					315					320
15	Arg	Gln	Ala	Thr	Ala	His	Cys	Pro	Asn	Ser	Tyr	Val	Asn	Asn	Asn	Asp
					325					330					335	
	Ile	Tyr	Gln	Val	Thr	Pro	Val	Tyr	Arg	Leu	Gly	Ser	Asn	Asp	Lys	Glu
				340					345					350		
	Ile	Met	Lys	Glu	Leu	Met	Glu	Asn	Gly	Pro	Val	Gln	Ala	Leu	Met	Glu
20			355					360					365			
	Val		Glu	Asp	Phe	Phe		Tyr	Lys	Gly	Gly	Ile	Tyr	Ser	His	Thr
		370					375					380				
		Val	Ser	Leu	Gly		Pro	Glu	Arg	Tyr		Arg	His	Gly	Thr	
0.5	385					390					395					400
25	Ser	Val	Lvs	Ile	Thr	Glv	Trp	Glv	Glu	Glu	Thr	Len	Pro	Asp	Glv	Ara

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Thr Leu Lys Tyr Trp Thr Ala Ala Asn Ser Trp Gly Pro Ala Trp Gly Glu Arg Gly His Phe Arg Ile Val Arg Gly Val Asn Glu Cys Asp Ile Glu Ser Phe Val Leu Gly Val Trp Gly Arg Val Gly Met Glu Asp Met Gly His His <210> 126 <211> 476 <212> PRT <213> Homo sapiens <400> 126 Met Ala Gly Ser Asp Thr Ala Pro Phe Leu Ser Gln Ala Asp Asp Pro Asp Asp Gly Pro Val Pro Gly Thr Pro Gly Leu Pro Gly Ser Thr Gly Asn Pro Lys Ser Glu Glu Pro Glu Val Pro Asp Gln Glu Gly Leu Gln Arg Ile Thr Gly Leu Ser Pro Gly Arg Ser Ala Leu Ile Val Ala Val Leu Cys Tyr Ile Asn Leu Leu Asn Tyr Met Asp Arg Phe Thr Val Ala

	65					70					75					80
	Gly	۷al	Leu	Pro	Asp	Ile	Glu	Gln	Phe	Phe	Asn	Ile	Gly	Asp	Ser	Ser
					85					90					95	
	Ser	Gly	Leu	Ile	Gln	Thr	Val	Phe	Ile	Ser	Ser	Tyr	Met	Val	Leu	Ala
5				100					105					110		
	Pro	Val	Phe	Gly	Tyr	Leu	Gly	Asp	Arg	Tyr	Asn	Arg	Lys	Tyr	Leu	Met
			115					120					125			
	Cys	Gly	Gly	Ile	Ala	Phe	Trp	Ser	Leu	Val	Thr	Leu	Gly	Ser	Ser	Phe
		130					135					140				
10	Ile	Pro	Gly	Glu	His	Phe	Trp	Leu	Leu	Leu	Leu	Thr	Arg	Gly	Leu	Val
	145					150					155					160
	Gly	Val	Gly	Glu	Ala	Ser	Tyr	Ser	Thr	Ile	Ala	Pro	Thr	Leu	Ile	Ala
					165					170					175	
	Asp	Leu	Phe	Val	Ala	Asp	Gln	Arg	Ser	Arg	Met	Leu	Ser	Ile	Phe	Tyr
15				180				•	185				·	190		
	Phe	Ala	Ile	Pro	Val	Gly	Ser	Gly	Leu	Gly	Tyr	Ile	Ala	Gly	Ser	Lys
			195					200					205			
	Val	Lys	Asp	Met	Ala	Gly	Asp	Trp	His	Trp	Ala	Leu	Arg	Val	Thr	Pro
		210					215					220				
20	Gly	Leu	Gly	Val	Val	Ala	Val	Leu	Leu	Leu	Phe	Leu	Val	Val	Arg	Glu
	225					230					235					240
	Pro	Pro	Arg	Gly	Ala	Val	Glu	Arg	His	Ser	Asp	Leu	Pro	Pro	Leu	Asn
					245					250					255	
	Pro	Thr	Ser	Trp	Trp	Ala	Asp	Leu	Arg	Ala	Leu	Ala	Arg	Asn	Leu	Ile
25				260					265					270		

	Phe	Gly	Leu	Ile	Thr	Cys	Leu	Thr	Gly	Val	Leu	Gly	Val	Gly	Leu	Gl.
			275					280					285			
	Val	Glu	Ile	Ser	Arg	Arg	Leu	Arg	His	Ser	Asn	Pro	Arg	Ala	Asp	Pro
		290					295				•	300				
5	Leu	Val	Cys	Ala	Thr	Gly	Leu	Leu	Gly	Ser	Ala	Pro	Phe	Leu	Phe	Let
	305					310					315					320
	Ser	Leu	Ala	Cys	Ala	Arg	Gly	Ser	Ile	Val	Ala	Thr	Tyr	Ile	Phe	Ile
					325				•	330					335	
	Phe	Ile	Gly	Glu	Thr	Leu	Leu	Ser	Met	Asn	Trp	Ala	Ile	Val	Ala	Ası
10				340					345					350		
	Ile	Leu	Leu	Tyr	Val	Val	Ile	Pro	Thr	Arg	Arg	Ser	Thr	Ala	Glu	Ala
			355	,				360					365			
	Phe	Gln	Ile	Val	Leu	Ser	His	Leu	Leu	Gly	Asp	Ala	Gly	Ser	Pro	Туг
		370					375					380				
15	Leu	Ile	Gly	Leu	Ile	Ser	Asp	Arg	Leu	Arg	Arg	Asn	Trp	Pro	Pro	Ser
	385					390					395					400
	Phe	Leu	Ser	Glu	Phe	Arg	Ala	Leu	Gln	Phe	Ser	Leu	Met	Leu	Cys	Ala
					405					410					415	
	Phe	Val	Gly	Ala	Leu	Gly	Gly	Ala	Ala	Phe	Leu	Gly	Thr	Ala	Ile	Phe
20				420					425					430		
	Ile	Glu	Ala	Asp	Arg	Arg	Arg	Ala	Gln	Leu	His	Val	Gln	Gly	Leu	Leu
			435					440					445			
	His	Glu	Ala	Gly	Ser	Thr	Asp	Asp	Arg	Ile	Val	Val	Pro	Gln	Arg	Gly
		450					455					460				
25	Arg	Ser	Thr	Arg	Val	Pro	Val	Ala	Ser	Val	Leu	Ile				

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<210> 127 <211> 449 <212> PRT <213> Homo sapiens <400> 127 Met Ser Asp Ile Arg His Ser Leu Leu Arg Arg Asp Ala Leu Ser Ala 5. Ala Lys Glu Val Leu Tyr His Leu Asp Ile Tyr Phe Ser Ser Gln Leu Gln Ser Ala Pro Leu Pro Ile Val Asp Lys Gly Pro Val Glu Leu Leu Glu Glu Phe Val Phe Gln Val Pro Lys Glu Arg Ser Ala Gln Pro Lys Arg Leu Asn Ser Leu Gln Glu Leu Gln Leu Leu Glu Ile Met Cys Asn Tyr Phe Gln Glu Gln Thr Lys Asp Ser Val Arg Gln Ile Ile Phe Ser Ser Leu Phe Ser Pro Gln Gly Asn Lys Ala Asp Asp Ser Arg Met Ser Leu Leu Gly Lys Leu Val Ser Met Ala Val Ala Val Cys Arg Ile Pro

Val Leu Glu Cys Ala Ala Ser Trp Leu Gln Arg Thr Pro Val Val Tyr

		130					135					140							
	Cys	Val	Arg	Leu	Ala	Lys	Ala	Leu	Val	Asp	Asp	Tyr	Cys	Cys	Leu	Val			
	145					150					155					160			
	Pro	Gly	Ser	Ile	Gln	Thr	Leu	Lys	Gln	Ile	Phe	Ser	Ala	Ser	Pro	Arg	*		
5					165					170					175				
	Phe	Cys	Cys	Gln	Phe	Ile	Thr	Ser	Val	Thr	Ala	Leu	Tyr	Asp	Leu	Ser			
				180					185					190					
	Ser	Asp	Asp	Leu	Ile	Pro	Pro	Met	Asp	Leu	Leu	Glu	Met	Ile	Val	Thr			
			195					200					205						
10	Trp	Ile	Phe	Glu	Asp	Pro	Arg	Leu	Ile	Leu	Ile	Thr	Phe	Leu	Asn	Thr			•
		210					215					220							ű
	Pro	Ile	Ala	Ala	Asn	Leu	Pro	Ile	Gly	Phe	Leu	Glu	Leu	Thr	Pro	Leu			
	225					230					235					240			
	Val	Gly	Leu	Ile	Arg	Trp	Cys	Val	Lys	Ala	Pro	Leu	Ala	Tyr	Lys	Arg			
15					245					250					255			•	
	Lys	Lys	Lys	Pro	Pro	Leu	Ser	Asn	Gly	His	Val	Ser	Asn	Lys	Val	Thr			
				260					265					270					
	Lys	Asp	Pro	Gly	Val	Gly	Met	Asp	Arg	Asp	Ser	His	Leu	Leu	Tyr	Ser			
			275					280					285						
20	Lys	Leu	His	Leu	Ser	Val	Leu	Gln	Val	Leu	Met	Thr	Leu	Gln	Leu	His			
		290					295					300							
	Leu	Thr	Glu	Lys	Asn	Leu	Tyr	Gly	Arg	Leu	Gly	Leu	Ile	Leu	Phe	Asp			
	305					310					315					320			
	His	Met	Val	Pro	Leu	Val	Glu	Glu	Ile	Asn	Arg	Leu	Ala	Asp	Glu	Leu			
25					325					33N					335				

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Asn Pro Leu Asn Ala Ser Gln Glu Ile Glu Leu Ser Leu Asp Arg Leu Ala Gin Ala Leu Gln Val Ala Met Ala Ser Gly Ala Leu Leu Cys Thr Arg Asp Asp Leu Arg Thr Leu Cys Ser Arg Leu Pro His Asn Asn Leu Leu Gln Leu Val Ile Ser Gly Pro Val Gln Gln Ser Pro His Ala Ala Leu Pro Pro Gly Phe Tyr Pro His Ile His Thr Pro Pro Leu Gly Tyr Gly Ala Val Pro Ala His Pro Ala Ala His Pro Ala Leu Pro Thr His Pro Gly His Thr Phe Ile Ser Gly Val Thr Phe Pro Phe Arg Pro Ile Arg <210> 128 <211> 105 <212> PRT <213> Homo sapiens <400> 128

Met Arg Arg Ile Ser Leu Thr Ser Ser Pro Val Arg Leu Leu Phe

	Leu Leu	Leu	Leu	Leu	Ile	Ala	Leu	Glu	Ile	Met	Val	Gly	Gly	His	Sei
			20					25					30		
	Leu Cys	Phe	Asn	Phe	Thr	Ile	Lys	Ser	Leu	Ser	Arg	Pro	Gly	Gln	Pro
		35					40					45			
5	Trp Cys	Glu	Ala	Gln	Val	Phe	Leu	Asn	Lys	Asn	Leu	Phe	Leu	Gln	Tyr
	50	)				55					60				
	Asn Ser	Asp	Asn	Asn	Met	Val	Lys	Pro	Leu	Gly	Leu	Leu	Gly	Lys	Lys
	65	,			70					75					80
	Val Asn	Ala	Thr	Ser	Thr	Trp	Gly	Glu	Asn	Pro	Asn	Ala	Gly	Arg	Ser
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			100					105							
	<210> 1	29													
15	<211> 8	1													
	<212> P	RT													
	<213> н	omo s	sapie	ens											
	<400> 1	29													
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	1			5					10					15	
	Arg Arg	Pro	Val	Pro	Val	Ala	Ala	Gly	Pro	Gly	Asp	Thr	Arg	Pro	Ala
			20					25					30		
_	Leu Leu	Ser	Phe	Glu	Ala	Pro	Val	Phe	Val	Pro	Thr	Leu	Thr	Pro	Gly
25		35					40					45			

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Cys Leu Gln Gln Pro Arg Gly Arg Asn Gly Ala Ser Pro Arg Gly Leu Leu Pro Gln Pro Leu Asp Gly Thr Ala Ala Ser Pro Val Cys His His Val <210> 130 <211> 552 <212> PRT <213> Homo sapiens <400> 130 Met Arg Arg Leu Thr Arg Arg Leu Val Leu Pro Val Phe Gly Val Leu Trp Ile Thr Val Leu Leu Phe Phe Trp Val Thr Lys Arg Lys Leu Glu Val Pro Thr Gly Pro Glu Val Gln Thr Pro Lys Pro Ser Asp Ala Asp Trp Asp Asp Leu Trp Asp Gln Phe Asp Glu Arg Arg Tyr Leu Asn Ala Lys Lys Trp Arg Val Gly Asp Asp Pro Tyr Lys Leu Tyr Ala Phe Asn Gln Arg Glu Ser Glu Arg Ile Ser Ser Asn Arg Ala Ile Pro Asp Thr

	Arg	His	Leu	Arg	Cys	Thr	Leu	Leu	Val	Tyr	Cys	Thr	Asp	Leu	Pro	Pro
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	Thr	Ser	Ile	Ile	Ile	Thr	Phe	His	Asn	Glu	Ala	Arg	Ser	Thr	Leu	Leu
			115					120					125			
5	Arg	Thr	Ile	Arg	Ser	Val	Leu	Asn	Arg	Thr	Pro	Thr	His	Leu	Ile	Arg
		130					135					140				
	Glu	<u>I</u> le	Ile	Leu	Val	Asp	Asp	Phe	Ser	Asn	Asp	Pro	Asp	Asp	Cys	Lys
	145					150					155					160
	Gln	Leu	Ile	Lys	Leu	Pro	Lys	Val	Lys	Cys	Leu	Arg	Asn	Asn	Glu	Arg
10					165					170					175	
	Gln	Gly	Leu	Val	Arg	Ser	Arg	Ile	Arg	Gly	Ala	Asp	Ile	Ala	Gln	Gly
				180					185					190		
	Thr	Thr	Leu	Thr	Phe	Leu	Asp	Ser	His	Cys	Glu	Val	Asn	Arg	Asp	Trp
			195					200					205			
15	Leu	Gln	Pro	Leu	Leu	His	Arg	Val	Lys	Glu	Asp	Tyr	Thr	Arg	Val	Val
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	Cys	Pro	Val	Ile	Asp	Ile	Ile	Asn	Leu	Asp	Thr	Phe	Thr	Tyr	Ile	Glu
	225					230					235					240
	Ser	Ala	Ser	Glu	Leu	Arg	Gly	Gly	Phe	Asp	Trp	Ser	Leu	His	Phe	Gln
20					245					250					255	
	Trp	Glu	Gln	Leu	Ser	Pro	Glu	Gln	Lys	Ala	Arg	Arg	Leu	Asp	Pro	Thr
				260					265					270		
	Glu	Pro	Ile	Arg	Thr	Pro	Ile	Ile	Ala	Gly	Gly	Leu	Phe	Val	Ile	Asp
			275					280					285			
25	Lys	Ala	Trp	Phe	Asp	Tyr	Leu	Gly	Lys	Tyr	Asp	Met	Asp	Met	Asp	Ile

		290					295					300				
	Trp	Gly	Gly	Glu	Asn	Phe	Glu	Ile	Ser	Phe	Arg	Val	Trp	Met	Суз	Gly
	305					310					315					320
	Gly	Ser	Leu	Glu	Ile	Val	Pro	Cys	Ser	Arg	Val	Gly	His	Val	Phe	Arg
5					325					330					335	
	Lys	Lys	His	Pro	Tyr	Val	Phe	Pro	Asp	Gly	Asn	Ala	Asn	Thr	Tyr	Ile
				340					345					350		
	Lys	Asn	Thr	Lys	Arg	Thr	Ala	Glu	Val	Trp	Met	Asp	Glu	Tyr	Lys	Gln
			355					360					365			
10	Tyr	Tyr	Tyr	Ala	Ala	Arg	Pro	Phe	Ala	Leu	Glu	Arg	Pro	Phe	Gly	Asn
		370					375					380				
	Val	Glu	Ser	Arg	Leu	Asp	Leu	Arg	Lys	Asn	Leu	Arg	Cys	Gln	Ser	Phe
	385					390					395				_	400
	Lys	Trp	Tyr	Leu	Glu	Asn	Ile	Tyr	Pro	Glu	Leu	Ser	Ile	Pro	Lys	Glu
15					405					410					415	
	Ser	Ser	Ile	Gln	Lys	Gly	Asn	Ile	Arg	Gln	Arg	Gln	Lys	Cys	Leu	Glu
				420					425					430		
	Ser	Gln	Arg	Gln	Asn	Asn	Gln	Glu	Thr	Pro	Asn	Leu	Lys	Leu	Ser	Pro
			435					440					445			
20	Cys	Ala	Lys	Val	Lys	Gly	Glu	Asp	Ala	Lys	Ser	Gln	Val	Trp	Ala	Phe
		450					455					460				
	Thr	Tyr	Thr	Gln	Gln	Ile	Leu	Gln	Glu	Glu	Leu	Суз	Leu	Ser	Val	Ile
	465					470					475					480
	Thr	Leu	Phe	Pro	Gly	Ala	Pro	Val	Val	Leu	Val	Leu	Cys	ГÀЗ	Asn	Gly
25		•			485					490					495	

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(4)

Asp Asp Arg Gln Gln Trp Thr Lys Thr Gly Ser His Ile Glu His Ile
500 505 510

Ala Ser His Leu Cys Leu Asp Thr Asp Met Phe Gly Asp Gly Thr Glu
515 520 525

5 Asn Gly Lys Glu Ile Val Val Asn Pro Cys Glu Ser Ser Leu Met Ser 530 535 540

Gln His Trp Asp Met Val Ser Ser

545 550

10 <210> 131

<211> 1188

<212> DNA

<213> Homo sapiens

15 <400> 131

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25

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teceteetet teecagtgaa gteagaacag gatgetggga actacteetg egaggetgag 720

aacagtgtet eeagagagag gagtgageee aagaagetgt etetgaaggg tteteaagte 780

ttgtteacte eegeeageaa etggetggtt eettggette etgegageet gettggeetg 840

atggttattg etgetgeact tetggtttat gtgagateet ggagaaaage tgggeeeett 900

ceateccaga taccaccaca ageteeaggt ggagageagt geeeactata tgeeaacgtg 960

cateaccaga aagggaaaga tgaaggtgtt gtetactetg tggtgeatag aaceteaaag 1020

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<210> 132

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10

20

25

<211> 1653

<212> DNA

15 <213> Homo sapiens

<400> 132

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<211> 657

<212> DNA

25 <213> Homo sapiens

#### 298/346

<400> 133

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15 <210> 134

<211> 1791

<212> DNA

<213> Homo sapiens

20 <400> 134

25

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<211> 1404

<212> DNA

5 <213> Homo sapiens

<400> 135

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<210> 136

<211> 1431

10 <212> DNA

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15

20

25

<213> Homo sapiens

<400> 136

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gggageeeet accteattgg eetgateete gaeegeetge geeggaaetg geeeeetee 1200
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<210> 137

15 <211> 1350

<212> DNA

<213> Homo sapiens

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gacaagggee cegtggaget getggaggag ttegtgttee aggtgeecaa ggagegeage 180

gegeageeca agagaetgaa tteeetteag gagetteaac ttettgaaat catgtgeaat 240

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25 ceteaaggga acaaageega tgacageegg atgagettgt tgggaaaact ggteteeatg 360

### 303/346

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L <b>5</b>	ctcccccgg	ggttctaccc	ccacatccac	acgcccccgc	tgggctacgg	ggctgtcccg	1260
	gcccaccccg	ccgcccaccc	cgccctgccc	acgcaccccg	gccacacctt	catctccggc	1320
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<212> DNA

<213> Homo sapiens

<400> 138

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	ttccttcagt	acaacagtga	caacaacatg	gtcaaacctc	tgggcctcct	ggggaagaag	240
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<212> DNA

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<212> DNA

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<400> 140

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10

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25

#### 305/346

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<212> DNA

<213> Homo sapiens

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ctgtctggct gtacctccaa gcctggccaa accctgtgtt tgaaggagat gccctgactc 180

tgcg atg tca ggg atg gaa gaa tac acc act gtc tca ggt gaa gtt cta 229

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1 5 10 15

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25 35 40 45

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5				Gln													
		65					70					75					
	tct	cct	gag	ccc	cga	gag		age	cta	ata	acc		202	tat	cac	202	469
				Pro													403
	80	-10	014	110	,mg	85	Gly	per	пец	val		ьец	Arg	cys	GIN		
10	•	~ h~									90					95	
10				ccc													517
	Lys	Leu	His	Pro	Leu	Arg	Ser	Ala	Leu	Arg	Leu	Leu	Phe	Ser	Phe	His	
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	Lys	Asp	Gly	His	Thr	Leu	Gln	Asp	Arg	Gly	Pro	His	Pro	Glu	Leu	Cys	
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	Ile	Pro	Gly	Ala	Lys	Glu	Gly	Asp	Ser	Gly	Leu	Tyr	Trp	Cys	Glu	Val	
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		145					150					155					
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				Ala													705
	160				<b>-</b>	165				* U.L.		111 <u>T</u>	.u∈u	1172	****	_	
25		ac+	~~~	00±			<b></b>				170					175	
	نانات	yct	yac	CCT	gct	grg	ggg	gac	atg:	gtg	cag	ctc	ctc	tgt	gag	gca	757

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	Glu	Asn	Ser	Val	Ser	Arg	Glu	Arg	Ser	Glu	Pro	Lys	Lys	Leu	Ser	Leu	
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	Lys	Gly	Ser	Gln	Val	Leu	Phe	Thr	Pro	Ala	Ser	Asn	Trp	Leu	Val	Pro	
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			cct												-		1045
	Trp	Leu	Pro	Ala	Ser	Leu	Leu	Gly	Leu	Met	Val	Ile	Ala	Ala	Ala	Leu	
. 20		•		275					280					285			
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	Val His His Gln Lys	Gly Lys Asp Glu	Gly Val Val Tyr Ser Val Val	
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5	cat aga acc tca aag	agg agt gaa gcc	agg tct gct gag ttc acc gtg	1237
	His Arg Thr Ser Lys	Arg Ser Glu Ala	Arg Ser Ala Glu Phe Thr Val	
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	ggg aga aag gac agt	tct atc atc tgt	gcg gag gtg aga tgc ctg cag	1285
	Gly Arg Lys Asp Ser	Ser Ile Ile Cys	Ala Glu Val Arg Cys Leu Gln	
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	ccc agt gag gtt tca	tcc acg gag gtg	aat atg aga agc agg act ctc	1333
	Pro Ser Glu Val Ser	Ser Thr Glu Val	Asn Met Arg Ser Arg Thr Leu	
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15	Gln Glu Pro Leu Ser	Asp Cys Glu Glu	Val Leu Cys	
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	tatatatgaa atagtcat	gt gccgcataac aac	catttcag tcagtgatag actgcataca	1742
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15	Met Ala Phe Ser Lys Leu Leu Glu Gln Ala Gly Gly Val Gly Leu Phe	:
•	1 5 10 15	
	cag acc ctg cag gtg ctc acc ttc atc ctc ccc tgc ctc atg ata cct	153
	Gln Thr Leu Gln Val Leu Thr Phe Ile Leu Pro Cys Leu Met Ile Pro	•
	20 25 30	
20	too cag atg oto otg gag aac tto toa goo goo ato coa ggo cac oga	201
	Ser Gln Met Leu Leu Glu Asn Phe Ser Ala Ala Ile Pro Gly His Arg	I
	35 40 45	
	tgc tgg aca cac atg ctg gac aat ggc tct gcg gtt tcc aca aac atg	g 249
	Cys Trp Thr His Met Leu Asp Asn Gly Ser Ala Val Ser Thr Asn Met	:
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	Cys	Leu	Gln	Leu	Ala	Val	Ala	Gly	Thr	Ser	Thr	Ile	Phe	Ala	Pro	Thr	
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WO 01/49728 PCT/JP00/09359 ·

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	Thr	Leu	Gln	Leu	Ala	Ala	Ser	Val	Pro	Phe	Phe	Ala	Ile	Ser	Leu	Ile	
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	Ser	Trp	Trp	Leu	Pro	Glu	Ser	Ala	Arg	Trp	Leu	Ile	Ile	Ъуs	Gly	Lys	
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25	Lys	Glu	Glu	Val	Ala	Ser	Ala	Lys	Glu	Pro	Ara	Ser	Val	Leu	Asp	Leu	

					325					330					335		
	ttc	tgc	gtg	ccc	gtg	ctc	cgc	tgg	agg	agc	tgc	gcc	atg	ctg	gtg	gtg	1113
	Phe	Cys	Val	Pro	Val	Leu	Arg	Trp	Arg	Ser	Суѕ	Ala	Met	Leu	Val	Val	
				340					345					350			
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	Asn	Phe	Ser	Leu	Leu	Ile	Ser	Tyr	Tyr	Gly	Leu	Val	Phe	Asp	Leu	Gln	
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	Ser	Leu	Gly	Arg	Asp	Ile	Phe	Leu	Leu	Gln	Ala	Leu	Phe	Gly	Ala	Val	
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	Asp	Phe	Leu	Gly	Arg	Ala	Thr	Thr	Ala	Leu	Leu	Leu	Ser	Phe	Leu	Gly	
	385					390					395					400	
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					405					410					415		
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	Leu	Ala	Asn	Met	Leu	Val	Pro	Gln	Asp	Leu	Gln	Thr	Leu	Arg	Val	Val	
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	Phe	Ala	Val	Leu	Gly	Lys	Gly	Cys	Phe	Gly	Ile	Ser	Leu	Thr	Суѕ	Leu	
			435					440					445				
	acc	atc	tac	aag	gct	gaa	ctc	ttt	cca	acg	cca	gtg	cgg	atg	aca	gca	1449
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25		450					455					460					

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	Ser (	Gln	Lys	Ser	Thr	Ala	Ala	Gln	Gly	Asn	Arg	Gln	Glu	Ala	Val	Thr	
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	Val (	Glu	Ser	Thr	Ser	Leu											
	545					550											
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315/346

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15 Met Lys His

1

aca ctg gct ctg ctg gct ccc ctg ctg ggc ctg ggc ctg ggc ctg gcc 165
Thr Leu Ala Leu Leu Ala Pro Leu Leu Gly Leu Gly Leu Gly Leu Ala

5 10 15

20 ctg agt cag ctg gct gca ggg gcc aca gac tgc aag ttc ctt ggc ccg 213

Leu Ser Gln Leu Ala Ala Gly Ala Thr Asp Cys Lys Phe Leu Gly Pro

20 25 30 35

gca gag cac ctg aca ttc acc cca gca gcc agg gcc cgg tgg ctg gcc 261
Ala Glu His Leu Thr Phe Thr Pro Ala Ala Arg Ala Arg Trp Leu Ala

25 40 45 50

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Ser Leu Trp Gly Leu Val Ser Asp Val Pro Gln Val Ser Thr Val Thr

200 205 210

cct cac cct cat gtg ccc ctg tga gcactgggcc cgggcaggac agagccgagt 795 Pro His Pro His Val Pro Leu

215

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10

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5

10

15

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95

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Leu Ala Leu Ala Trp Val Phe Val Pro Ile Tyr Ile Ser Ser Glu Ile

100

90

25

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	Arg	Met	Tyr	Leu	Ser	Val	Leu	Ser	Leu	Leu	Leu	Ser	Val	Phe	Thr	Lys	
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323/346

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324/346

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10 Met Trp Arg Cys Pro

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ctg ggg cta ctg ctg ttg ctg ccg ctg gct ggc cac ttg gct ctg ggt 162
Leu Gly Leu Leu Leu Leu Pro Leu Ala Gly His Leu Ala Leu Gly

15 20

gcc cag cag ggt cgt ggg cgc cgg gag cta gca ccg ggt ctg cac ctg 210

Ala Gln Gln Gly Arg Gly Arg Glu Leu Ala Pro Gly Leu His Leu

25 30 35

cgg ggc atc cgg gac gcg gga ggc cgg tac tgc cag gag cag gac ctg 258
Arg Gly Ile Arg Asp Ala Gly Gly Arg Tyr Cys Gln Glu Gln Asp Leu

20 40 45 50

10

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55 60 65

atc tgt tac tgt gac ctc ttc tgc aac cgc acg gtc tcc gac tgc tgc 354

25 Ile Cys Tyr Cys Asp Leu Phe Cys Asn Arg Thr Val Ser Asp Cys Cys

325/346

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# 332/346

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cgggggccgc ggcggccgca cc atg agc gac atc cgc cac tcg ctg ctg cgc 292

Met Ser Asp Ile Arg His Ser Leu Leu Arg

15 1 5 10

15

cgc gat gcg ctg agc gcc gcc aag gag gtg ttg tac cac ctg gac atc 340 Arg Asp Ala Leu Ser Ala Ala Lys Glu Val Leu Tyr His Leu Asp Ile

20 25

tac ttc agc agc cag ctg cag agc gcg ccg ctg ccc atc gtg gac aag 388

20 Tyr Phe Ser Ser Gln Leu Gln Ser Ala Pro Leu Pro Ile Val Asp Lys

30 35 40

ggc ccc gtg gag ctg ctg gag gag ttc gtg ttc cag gtg ccc aag gag 436 Gly Pro Val Glu Leu Leu Glu Glu Phe Val Phe Gln Val Pro Lys Glu

45 50 55

25 cgc agc gcg cag ccc aag aga ctg aat tcc ctt cag gag ctt caa ctt 484

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	Arg	Gln	Ile	Ile	Phe	Ser	Ser	Leu	Phe	Ser	Pro	Gln	Gly	Asn	Lys	Ala	
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	Leu	Glu	Met	Ile	Val	Thr	Trp	Ile	Phe	Glu	Asp	Pro	Arg	Leu	Ile	Leu	
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<213> Homo sapiens

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25 15 20 25

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<213> Homo sapiens

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<221> CDS

<222> (227)..(472)

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Met Ser Pro

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10	cag cca	cgt	ggc	cga	aat	gga	gcc	tct	cca	cgg	ggg	ctc	ctt	ccc	cag	427
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	gtgctga	act o	gecea	ataa	a to	caca	agta	aga	igttg	caa	gaag	gago	ca a	aaaag	ggctg	892
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<222> (357)..(2015)

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ggetgeete ggteettee tgeeaegtt egggtegee tgeaeeeee acceaggete 180

gettetette gaageggaa gggegeettg eaggateetg eegeeetee aaceggatee 240

tgggtetaga geteeeeag gegaggeget egeeaggaet eetgeeeege eaaeeetgae 300

egeegggggg tgeeeeggg aegtagegee geggagagga ageggeaaag gggace atg 359

Met

1

20 cgg cgc ctg act cgt cgg ctg gtt ctg cca gtc ttc ggg gtg ctc tgg 407

Arg Arg Leu Thr Arg Arg Leu Val Leu Pro Val Phe Gly Val Leu Trp

10 15

atc acg gtg ctg ctg ttc ttc tgg gta acc aag agg aag ttg gag gtg 455

Ile Thr Val Leu Leu Phe Phe Trp Val Thr Lys Arg Lys Leu Glu Val

25 20 25 30

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	Arg Glu	Ser	Glu	Arg	Ile	Ser	Ser	Asn	Arg	Ala	Ile	Pro	Asp	Thr	Arg	
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	His Leu	Arg	Cys	Thr	Leu	Leu	Val	Tyr	Cys	Thr	Asp	Leu	Pro	Pro	Thr	
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	Thr	Leu	Thr	Phe	Leu	Asp	Ser	His	Cys	Glu	Val	Asn	Arg	Asp	Trp	Leu	
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10	Gln	Pro	Leu	Leu	His	Arg	Val	Lys	Glu	Asp	Tyr	Thr	Arg	Val	Val	Cys	
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	Pro	Val	. Ile	Asp	Ile	Ile	Asn	Leu	Asp	Thr	Phe	Thr	Tyr	Ile	Glu	Ser	
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	Pro	Il.	e Ar	g Thi	r Pro	Ile			a Gly	Gl	/ Lei			L Ile	e Asp	o Lys	
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	Ser	His	Leu	Cys	Leu	Asp	Thr	Asp	Met	Phe	Gly	Asp	Gly	Thr	Glu	Asn	
		515					520					525					
	ggc	aag	gaa	atc	gtc	gtc	aac	cca	tgt	gag	tcc	tca	ctc	atg	agc	cag	1991
20	Gly	Lys	Glu	Ile	Val	Val	Asn	Pro	Cys	Glu	Ser	Ser	Leu	Met	Ser	Gln	
	530					535					540					545	
	cac	tgg	gac	atg	gtg	agc	tct	tga	ggad	ccct	.gc (	cagaa	agcag	jc aa	agggo	catg	2045
	His	Trp	Asp	Met	Val	Ser	Ser										
					550												
25	ggat	ggto	act t	ccci	tggad	c ac	raaca	agact	. gga	aact	aga	cado	caagg	ao o	ectad	caacca	2105

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cctcagacat	cctggactgg	gaggtggagg	cagagccccc	caggacagga	gcaactgtct	2165
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totttccaaa	agaaataaa	g agaaactta	ıa			243